## JS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION Attorney Docket P1957R1

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## DS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION Reilly et al. Attorney Docket P1957R1

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CCAGCGACAT GGTCGCTGTA GGCTTCTATC CCGAAGATAG CCTGGTCAAA GGACCAGTTT × > GCCTGACCTG CGGACTGGAC H į. AACCAGGTCA TIGGICCAGI > o GATGACCAAG CTACTGGTTC × H Σ GGGCCCTTCT CCCGGGAAGA ω C æ CTGCCCCCAT GACGGGGGTA ρ, ri Pi CCACATGTGG GGTGTACACC > GAGAACCACA CTCTTGGTGT ۵, 2701 377

GTCGTTCGAG CAGCAAGCTC TCTTCCTCTA AGAAGGAGAT CTGCCGAGGA GACGGCTCCT Ö GCTGGACTCC CGACCTGAGG Ŋ Δ ᆸ CGCCTCCCGT GCGGAGGCA > Д TACAAGACCA ATGTTCTGGT E٠ E-4 × GGAGAACAAC CCTCTTGTTG z z M ATGGGCAGCC TACCCGTCGG œ Ö TGGGAGAGCA ACCCTCTCGT CGCCGTGGAG GCGGCACCTC 囟 > 4 2801 410

GAGAGGGACA CICICCCIGI GCAGAAGAGC CGTCTTCTCG × ACCACTACAC TGGTGATGTG >4 H GCTCTGCACA CGAGACGTGT Ħ ы GATGCATGAG CTACGTACTC £43 Ħ Σ CATGCTCCGT GTACGAGGCA ۸ د O TTGCAGAAGA AACGTCTTCT Ġ N V GCAGCAGGGG CGTCGTCCCC Ö o TCTCGTCCAC AGAGCAGGTG Ø TGGCACCTGT ACCGTGGACA × TVD 2901 443

TATCATCGAT AAACTGTCGA ATAGTAGCTA TTTGACAGCT AATTGAGTAC TTAACTCATG AAAAAATAAC TTTTTATTG CTCAGGGATT GCGAGCCAAC GGCGGCCCGC ರಿದಿರಿದಿರಿದಿದ್ದರು CGCTCGGTTG GAGTCCCTAA TATTCGTACG CTGCCGGGAT GACGGCCCTA ATAAGCATGC CTCCGGGTAA GAGGCCCATT ,p., 3001 477

lambda terminator

GGCACCGTCA ATGCGCTCAT CGTCATCCTC TGGCACATAC TTTAGATTGT TACGCGAGTA GCAGTAGGAG AAATCTAACA GCAGTCAGGC ACCGTGTATG CGTCAGTCCG TTAACGATTG AATTGCTAAC ITCGAAATTA CGCCATCAAA TAGTGTCAAT GCGGTAGTTT ATCACAGTTA AAGCTTTAAT 3101

GCCGGGCCTC TTGCG CGGCCCGGAG AACGC TGCCGGTACT ACGGCCATGA GGCTTGGTTA GGGACCTACG ACATCCGTAT CCGAACCAAT TGTAGGCATA CCCTGGATGC 3201

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FIG. 4D

Inventor: REILLY ET AI Docket No.: 11669,195USU1

Title: METHODS AND COMPOSITIONS

GAATICAACT ICICCATACT ITGGATAAGG AAATACAGAC ATGAAAAATC ICATIGCTGA GITGITAITT AAGCIIGCCC AAAAAGAAGA AGAGICGAAT CITAAGIIGA AGAGGIAIGA AACCIAIICC IIIAIGICIG IACIIIIIAG AGIAACGACI CAACAAIAAA IICGAACGGG IIIIICIICI ICICAGCIIA GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTGATTGAT CAGGTAGAGG CTIGACACAC GOGICCAICI ICGAAACCIC IAAIAGCAGI GACGIIACGA AGCGIIAIAC CGCGIIIIAC IGGIIGICGC CAACIAACIA GICCAICICC 101

GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TIGAAGCATC CTCGTCAGTA CCGCGACAT GCTCCATITC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TITCTICAAT AACTICGTAG GAGCAGICAI 201

AAAAGTTAAT CTTTTCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TJJGTAACTA GTACGCAAGT ITTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA 301

TCACGIAAAA AGGGIATCIA GAATIAIGAA GAAGAATAIC GCATIICIIC IIGCAICIAI GIICGIIIII ICIAIIGCIA CAAACGCGIA CGCIGAIAIC AGTGCATITI TCCCATAGAT CITAATACIT CITCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTITGCGCAT GCGACTATAG Anti-Tissue Factor Light Chain? >-~ ~ SIAI رب ح د S K AFLL Signal Sequence TIR-1 r z x STII × 40.1

GIGGIAGIGG ACGICICGGI CAGCCCIGIA GIÍCICGAIA GACTIGACCA GCCTCTGTGG GCGATAGGGT CACCATCACC TGCAGAGCCA GTCGCGACAT CAAGAGCTAT CTGAACTGGT œ ح س س ⊢ CGGAGACACC CGCTATCCCA > ∝ Ω > S 4 CICCCIGICC GAGGGACAGG S .\_ CAGATGACCC AGTCCCCGAG TCAGGGGCTC œ GTCTACTGGG Σ 0 501 26

CGAGGCTTTC ATGACTAAAT GATACGATGA TCAGAGCGAC TTCCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCTG 601 ATCAACAGAA ACCAGGAAAA GCTCCGAAAG TACTGATTTA CTATGCTACT AGTCTCGCTG AAGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC œ ဟ გ. > SLAE ~ >-1 7 ۵. TGGTCCTTTT **IAGTIGICTT** 0 9

TGTCCCATGG CTCAGAGGTA CCTGTAAACC GAGTCTCCAT GGACATTTGG ۵, ဟ TCAGCACGGA CGGTCTTCTG AAGCGTTGAA TAATGACAGA AGTCGTGCCT × TTCGCAACTT ATTACTGTCT ں. >-٠ ۲ 4 GCCAGAAGAC CTGACCATCA GCAGTCTGCA CCTAATGTGA GACTGGTAGT CGTCAGACGT J ₽ GGATTACACT 701 S

Inventor: REILLY ET AL. Docket No.: 11669.195USU1

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CACACGGACG \_ ACGAAGACAA S TOTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TTAGACCTTG ပ S CTCGTCAACT J ഫ CGGTAGACTA Ω S a. AGTAGAAGGG Ĺ GGTAGACAGA S ACACCGACGT 4 æ > TCAMACGAAC AGTTTGCTTG ∝ 801 AAGGTGGAGA TTCCACCTCT W > × 126

GICACAGAGC AGGACAGCAA TCCTGTCGTT Δ CAGTGTCTCG ப ٢ GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GCCCATTGAG GGTCCTCTCA တ W 0 S z ပ CCACCTATTG CGGGAGGTTA 0 \_ ~ z 0 > CICCGGIIIC AIGICACCII 3 0 × æ CTATCCCAGA GATAGGGTCT ۵, ACTIATIGAA TGAATAACTT z 901 160

TCACCCATCA GGGCCTGAGC AGTGGGTAGT CCCGGACTCG 0 CANAGICIAC GCCIGCGAAG CGGACGCTTC Œ ပ GTTTCAGATG >-> × AAAGCAGACT ACGAGAAACA TGCTCTTTGT × × ω TTTCGTCTGA Q 4 GACGCTGAGC CTGCGACTCG လ ٦ د GCAGCACCCT CGTCGTGGGA ٦ ٦ S TACAGCCTCA CCTGTCGTGG ATGTCGGAGT ဟ GGACAGCACC ⋳ ഗ Ω 1001 193

CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA TCCGGATTGC ပ ய GTTGTCCCCT ပ œ z 1101 TCGCCCGTCA CAAAGAGCTT GTTTCTCGAA S AGCGGGCAGT > ഗ 226

TTATCGTCAC TGCAATGCTT CGAAACCTCT AATAGCAGTG CICGGIIGCC GCCGGCGII IIIIAIIGII GCCGACGCGC AICICGAAIG AACIGIGIG GCAGGIAGAA GCIIIGGAGA CGTCCATCTT GAGCCAACGG CGGCCCGCAA AAAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACG 1201

CGCAATATGG CGCAAAATGA CCAACAGCGG TIGATTGATC AGGTAGAGGG GGCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG GCGTTATACC GCGTTTTACT GGTTGTCGCC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTCG GGCTACGGTC GTAAGGACTG CTGCTATGCC 1301

CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT TCGACGACGC GCTAATGCAT AGCTGCTGCG 1401

ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA 1501 TAGTCGCTTT GTTTTTATTT TITAATGTAT TIGTAACTAG TACGCAAGTT CACGTAAAAA GGGTATCTAG AATTATGAAG AÄGAATATCG CATTTCTTCT X N N N N L L ×

STII Signal Sequence TIR-1

# FIG. 1B

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S

GAGTGAGGCA CTCACTCCGI  $\alpha$ \_ AGCCAGGGG COGTCCCC ပ Q. GCCTGGTGC CCGGACCACG > \_ ပ Heavy Chain GTCTGGCGGT CAGACCGCCA ပ S Anti-Tissue Factor GCTGAGGTTC AGCTGGTGGA TCGACCACCT > .. CGACTCCAAG > ഥ ~ CTATTGCTAC AAACGCGTAC TTTGCGCATG >-4 z GATAACGATG 4 TTCGTTTTTT AAGCAAAAAA S Ç., > TGCATCTATG ACGTAGATAC Σ တ æ 1601 2

**AACTAACTAG** TTGATTGATC ATGGGTTGGA TACCCAACCT GCCCCGGGTA AGGGCCTGGA TCCCGGACCT CGGGGCCCAT GGTCCGTCAG CCAGGCAGTC > ACATGCACTG TGTACGTGAC 3 TTCCTCATGA AAGGAGTACT GAAGTTATAA CTTCAATATT CAGCTTCTGG GTCGAAGACC ഗ TTGTCCTGTG AACAGGACAC O S 1701 3

TGAACAGCCT TACCTGCAGA ပ > AAACACAGCA . ပ ACAATTCCAA ပ Ω, ATAAGCGCTG 0 œ CCGTGCCACT × Σ AGTICCAGGA >w TATGACCCGA z ſ., CAACACGATC S 4 CAGAGCAAGG

ACTTGTCGGA S ATGGACGTCT TTTGTGTCGT ~ **(-**z TGTTAAGGTT × ဟ z TATTCGCGAC ~ တ GGCACGGTGA **(-**4 œ TCAAGGTCCT Ω 0 <u>(</u>... ATACTGGGCT ۵. 0 > GTTGTGCTAG ← z GTCTCGTTCC G 0 w 1801 77

GAGCCGGAGG CTCGGCCTCC z က TCACCGTCTC AGTGGCAGAG 0 > **(--**GGAACCCTGG CCTTGGGACC د۔  $\leftarrow$ CTGGGGTCAA GACCCCAGTT 0 ပ 3 ACTTCGACTA TGAAGCTGAT >-Ω Ĺ TGCCGGCGAA ACGGCCGCTT 4 4 ACGAGCTCTG TGCTCGAGAC Ω **∝** Ø TCTATTATTG AGATAATAAC C >->-CTGTGACGGC GACACTGCCG ~  $\vdash$ 0 GCGTGCTGAG CGCACGACTC æ œ 1901 110

AAGGGGCTTG TTCCCCGAAC a CAAGGACTAC GTTCCTGATG Ω CGACGGACCA GCTGCCTGGT \_ O CGCCGGGACC GCGCCCTGG \_ 4 TGGGGGCACA ACCCCCGTGT ပ ပ CCCTCCTCCA AGAGCACCTC TCTCGTGGAG S  $\leftarrow$ S GGGAGGAGGT S S CCCCCTGGCA GGGGGACCGT 4 ... ۵, CATCGGTCTT GTAGCCAGAA > S ACCAAGGGCC TGGTTCCCGG ပ × 2001

GCAGCGTGGT CGTCGCACCA > > TACTCCCTCA ATGAGGGAGT \_ S CTCAGGACTC GAGTCCTGAG ... ပ S TCCTACAGTC AGGATGTCAG S 0 ... AAGGGCCGAC Trecesere 4 ۵. GCACGTGTGG CGTGCACACC  $\leftarrow$ = > TGACCAGCGG ACTGGTCGCC ပ S €--TCAGGGGCCC AGTCCGCGGG .\_ æ ၒ GTCGTGGAAC CAGCACCTTG z 3 S CGGTGACGGT GCCACTGCCA 2101 177

CGGGTTTAGA GCCCAAATCT × AGAAAGTTGA TOTITCAACT > ¥ AAGGTGGACA TTCCACCTGT Ω > × CAGCAACACC GTCGTTGTGG €-z ഗ TGCAACGTGA ATCACAAGCC TAGTGTTCGG ¥ = ACGITGCACT > z GACCTACATC CTGGATGTAG >-٤¬ TGGGCACCCA ACCCGTGGGT O ۲ ပ TCTAGCAGCT AGATCGTCGA S ഗ GACTGTGCCC CTGACACGGG ۵, >  $\vdash$ 2201 210

ACCCTCATGA ... TCCCCCCAAA ACCCAAGGAC TGGGTTCCTG × AGGGGGTTT Ω, ۵. GTCTTCCTCT CAGAAGGAGA د Œ, > GGGACCGTCA CCCTGGCAGT ഗ ი. ც TTGAGGACCC AACTCCTGGG ပ r. L CCAGCACCTG GGTCGTGGAC ω Ω. ~ CCCACCGTGC GGGTGGCACG O Ω, ۵, CTCACACATG GAGTGTGTAC =TGTGACAAAA ACACTGTTT Δ 2301 243

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AGGTGCATAA CAAGGAGTAC TCCACGTATT GTTCCTCATG × w > GACGCCCTGG CTGCCGCACC GCCTGAATGG CCGACTTACC G > z ပ \_ GTGGTCCTGA CTGGTACGTG GACCATGCAC CACCAGGACT > Ω > 0 3 = CACCGTCCTG GTGGCAGGAC TCAAGTTCAA ACTICAAGIT z \_ Ç, > × ← AGTCGCAGGA CTGGGACTCC TCAGCGTCCT GACCCTGAGG \_ ω > ۵, ഗ TACCGTGTGG ATGGCACACC GAGCCACGAA CTCGGTGCTT Œ > × **∝** ഗ GTTGTCGTGC TGCCAAGACA AAGCCGCGGG AGGAGCAGTA CAACAGCACG TGGTGGACGT ACCACCTGCA ۲ Ω ဟ > Z. CCCTGAGGTC ACATGCGTGG TGTACGCACC TCCTCGTCAT > > 0 ပ W GGGACTCCAG TTCGCCCCC £ > œ w ۵. ρ, × TCTCCCGGAC AGAGGGCCTG ACGGTTCTGT œ 2501 2401 277 310

TGGGACGGG ACCCTGCCCC ۵. ٦ ٦ ACAGGTGTAC TGTCCACATG > CCCGAGAACC GGCTCTTGG Œ œ AAAGGGCAGC TTTCCCGTCG 0 ပ CTCCAAAGCC GAGGTTTCGG ~ × S TCTTTTGGTA AGAAAACCAT ٤-× GCCCCCATCG CGGGGGTAGC ω -A . AGCCCTCCCA TCGGGAGGGT ۵. ... ~ TCTCCAACAA AGAGGTTGTT z ဟ AAGTGCAAGG TTCACGTTCC × U × 2601

GCAATGGGCA CGTTACCCGT 0 ပ z GAGTGGGAGA CTCACCCTCT W 3 CATCGCCGTG GTAGCGGCAC > ~ ATCCCAGCGA TAGGGTCGCT Ω တ ۵. AAAGGCTTCT TTTCCGAAGA Œ. ပ TCAGCCTGAC CTGCCTGGTC GACGGACCAG > \_ J AGTCGGACTG \_ တ AAGAACCAGG TTCTTGGTCC 0 z AGAGATGACC TCTCTACTGG Σ ω CATCCCGGGA GTAGGGCCCT ø, ഗ 2701

GTGGCAGCAG CACCGTCGTC 0 3 ACAAGAGCAG TOTICICATO ഗ CTCACCGTGG GAGTGGCACC > **(-**CTACAGCAAG GATGTCGTTC × S >-CCTTCTTCCT GGAAGAAGGA .. G. Çe. AGGCTGCCGA TCCGACGGCT ပ 0 GCACGACCTG CGTGCTGGAC 0 ر د CCACGCCTCC GGTGCGGAGG Ω, ۵. ₽ AACTACAAGA TTGATGTTCT × >-GCCGGAGAAC CGCCTCTTG z w ۵. 2801 410

TAMATAMECA TECENCECC ATTTATTCGT TGTCTCCGG ACAGAGGCCC ۵. S AGCCTCTCCC TCGGAGAGGG S ... S GAGGCTCTGC ACAACCACTA CACGCAGAAG GTGCGTCTTC × 0 **-**TGTTGGTGAT **>**-I z CTCCGAGACG \_ æ CGTGATGCAT GCACTACGTA  $\equiv$ Σ > TCTCATGCTC AGAGTACGAG ഗ ပ S CCCTTGCAGA GGGAACGTCT > z O 2901 443

TTTATCACAG ANTAGTGTC AATGCGGTAG CCCAAAAAAT AACAATIGAG TACAAACTGT CGAATAGTAG CTATTCGAAA TTACGCCATC GATAAGCTTT GCTTATCATC TIGITAACIC AIGITIGACA GCGTTTTTTA TTGCCGCCGG AACGGCGGCC ATTGCGAGCC TAACGCTCGG SATCTCAGGG CTAGAGTCCC 3001

ATAGGCTTGG TATCCGAACC TGCTGTAGGC ACGACATCCG TCACCCTGGA AGTGGGACCT CATCGTCATC CTCGGCACCG GTAGCAGTAG GAGCCGTGGC Coding Sequence ACAATGCGCT TGTTACGCGA Resistance ATGAMATCTA TACTTTAGAT Start Tet GGCACCGTGT CCGTGCCACA AACGCAGTCA TIGCGICAGI TTANATIGCT ATTTACGA 3101

CTATATGCGT TGATGCAATT CGACGATCGC GATATACGCA ACTACGTTAA GCTGCTAGCG ATCGCCAGTC ACTATGGCGT TAGCGGTCAG TGATACCGCA TTCCGACAGC AAGGCTGTCG ATATCGTCCA TATAGCAGGT CTCTTGCGGG TGACGCCCG GAGAACGCCC ACTGCCGGGC TTATGCCGGT AATACGGCCA 3201

# FIG. 1D

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CAGGTAGAGG INGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GITGITAITT AAGCTTGCCC AAAAGAAGA AGAGTCGAAT TCGADACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC TITATGICIG TACTITITAG AGTAACGACT CAACAATAAA TICGAACGGG TITITICITCI GTTGATTGAT ACCAACAGCG GCGCAAAATG TCGCAATATG CTGCAATGCT ATTATCGTCA AGAGGTATGA AACCTATTCC AGCTTTGGAG TCTCCATACT CGCAGGTAGA GCGTCCATCT GAATTCAACT CTTGACACAC CITAAGITGA GAACTGTGTG 101

CTCGTCAGTA CGCTAATGCA TITCTICAAI AACTICGIAG GAGCAGICAI TTGAAGCATC CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA CTCGACGACG GGGCTACGGT CGTAAGGACT GCTGCTATGC CGAGGTAAAG CCCGATGCCA GCATTCCTGA GCTCCATTTC GGCGCTGTA CCCGCGACAT 201

ITITCAATTA GAAAAGITIGI CGACAGIAIT ICAACAGIGC CGGCICIGAA IAICAGCGAA ACAAAAAIAA AAAAITACAI AAACAÍTGAI CAIGCGITCA 301 AAAAGTTAAT CTTTTCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTAAT TTTTAATGTA TTTGTAACTA GTACGCAAGT

TCACGTAAAA AGGGTATCTA GAATTATGAA GAAAACATC GCTTTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC agtgcatttt tcccatagat cttaatactt ctttttgtag cgaaaagaag aacgtagata caagcaaaaa agataacgat gtttg¢gcat gcgactatag start light chain Çe, F V Σ တ Ø .1 \*start STII signal TIR-2 401

GIGGIAGIGG ACGICICGGI CAGCGCIGIA GITCIÓGAIA GACTIGACCA CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CACCATCACC TGCAGAGCCA GTCGCGACAT CAAGAGCTAT CTGAACTGGT × Ω œ æ œ H  $\vdash$ ₽ CGGAGACACC CGCTATCCCA œ Ω တ GAGGGACAGG ഗ .7 S 501 CAGATGACCC AGTCCCGGAG TCAGGGGCTC Ω, S GTCTACTGGG ⋳ Σ o 26

CGAGGCTTTC ATGACTAAAT GATACGATGA TCAGAGCGAC TTCCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCTTG ATCAACAGAA ACCAGGAAAA GCTCCGAAAG TACTGATTTA CTATGCTACT AGTCTCGCTG AAGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC G ∝ ഗ 20 SLA YAY 1 1 × a A TGGTCCTTTT ပ ۵. TAGTIGICTI 601 9

GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA GAGTCTCCAT GGACATTGG ACAGGGTACC TGTCCCATGG ტ o AAGCGTTGAA TAATGACAGA AGTCGTGCCT CTCAGAGGTA CCTGTAAACC ۵. S Ö × o X C FATY CGGTCTTCTG <u>а</u> ρ, CGTCAGACGT S GACTGGTAGT T T CCTAATGTGA 701 33

GTGTGCCTGC AGTITIGCITIG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGGACG TCATCTICCC GCCATCTGAT GAGCAGTIGA AATCTGGAAC IGCTTGTGTT S Ø ပ တ **ار** ح o Ω ഗ E G CCATCTGTCT တ TGTGGCTGCA **A** > TCAAACGAAC AAGGTGGAGA TICCACCICI ш > × 801 126

# FIG. 2A

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CCAGGAGAGT GTCACAGAGC AGGACAGCAA cadierere recrerent GGTCCTCTCA W o CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC GCCCATTGAG z G CGGGAGGTTA o CCACCTATTG Ω > CICCGGIITC AIGICACCIT 3 o Ø GATAGGGTCT Ω, TGAATAACTT ACTIATIGAA z 901 160

TCACCCATCA GGGCCTGAGC CCCGGACTCG ဗ AGTGGGTAGT CAAAGTCTAC GCCTGCGAAG CGGACGCTTC Œ ပ æ GTTTCAGATG > > × GACGCTGAGC AAAGCAGACT ACGAGAAACA TGCTCTTTGT I × ω TTTCGTCTGA Ω æ × CTGCGACTCG တ ... TACAGCCTCA GCAGCACCCT CGTCGTGGGA H ₽ ഗ ATGTCGGAGT L S GGACAGCACC CCTGTCGTGG ₽ S Ω 1001 193

TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCTAGA TCCGGATTGC 0 ပ ω GTTTCTCGAA GTTGTCCCCT O æ z Ç£, တ × AGCGGGCAGT > လ 1101 226

CTCGGTTGCC GCCGGCGTT ITTATTGTT GCCGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA ITATCGTCAC TGCAATGCTT BAGCCAACGG CGGCCCGCAA AAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA 1201

CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GGCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG GTAAGGACTG CTGCTATGCC CTCCATTTCG GGCTACGGTC CCGCGACATG TCCATCTCCC GGTTGTCGCC AACTAACTAG GCGTTTTACT CGCAATATGG SCGTTATACC 1301

AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA ICGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACÁGTGCC GGCTCTGAAT 1401

GAAAAGAAGA TITAATGTAT TIGTAACTAG TACGCAAGIT CACGTAAAAA GGGTAICTAG AAITAIGAAG AAAAACAICG CITITCTICI H L Çz, TTTTTGTAGC z CCCATAGATC TTAATACTTC × ATCAGCGADA CAAAAAAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT 1501 TAGTCGCTTT GTTTTTATTT

start heavy chain

GAGTGAGGCA CTCACTCCGI

GCCTGGTGC AGCCAGGGGG cceaccace reericcec

GTCTGGCGGT CAGACCGCCA

1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGCGTAC GCTGAGGTTC AGCTGGTGGA

ACGIAGAIAC AAGCAAAAA GAIAACGAIG ITIGCGCAIG CGACICCAAG ICGACCACCI

STII signal

start

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AACTAACTAG TTGATTGATC TGAACAGCCT ACTIGICGGA L ഗ z ATGGGTTGGA TACCTGCAGA TACCCAACCT ATGGACGTCT G O > 3 GCCCCGGGTA AGGGCCTGGA TTTGTGTCGT TCCCGGACCT AAACACAGCA ĿЗ 4 J ₽ G z CGGGCCCCAT ACAATTCCAA TGTTAAGGTT  $\simeq$ Ö ഗ ۵, z K ATAAGCGCTG GGTCCGTCAG CCAGGCAGTC TATTCGCGAC Ω O 4 œ လ > AAGGAGTACT ACATGCACTG CCGTGCCACT GGCACGGTGA TGTACGTGAC 3 ₽ × æ Σ 04 TTCCTCATGA AGTTCCAGGA TCAAGGTCCT Ω >-O ш Œ CTTCAATATT TATGACCCGA GAAGTTATAA ATACTGGGCT ۵, Z Ω Œ, CAGCTTCTGG GTTGTGCTAG GTCGAAGACC CAACACGATC G S E æ z TTGTCCTGTG CAGAGCAAGG AACAGGACAC GTCTCGTTCC G O 0 လ (L) H 1801 43 77

1701

CICGGCCICC GAGCCGGAGG ഗ ഗ TCACCGTCTC AGTGGCAGAG ₽ GGAACCCTGG CCTTGGGACC L ₽ G TGCTCGAGAC ACGCCGCTT ACTTCGACTA CTGGGGTCAA GACCCCAGIT O G 3 TGAAGCTGAT  $\rightarrow$ Ω Cz. TGCCGGCGAA æ Ø ⊢ ACGAGCTCTG Ω œ 4 TCTATTATTG AGATAATAAC U >->-GACACTGCCG CTGTGACGGC æ GCGTGCTGAG CGCACGACTC ω æ  $\alpha$ 1901 110

TTCCCCGAAC AAGGGGCTTG Ω, GTTCCTGATG CAAGGACTAC > × CGACGGACCA GCTGCCTGGT .\_ O GCGCCCTGG CGCCGGGACC L æ TGGGGGCACA ACCCCCGTGT E Ö G TCTCGTGGAG CCCTCCTCCA AGAGCACCTC ₽ တ GGGAGGAGGT × S S ρ, CCCCCTGGCA GGGGGACCGT æ L Ω, GTAGCCAGAA CATCGGTCTT > S ACCAAGGGCC TGGTTCCCGG G ₽ 2001 143

CGTCGCACCA GCAGCGTGGT > ഗ TACTCCCTCA ATGAGGGAGT S ... S GAGTCCTGAG CTCAGGACTC H ဗ ഗ AAGGGCCGAC AGGATGTCAG TCCTACAGTC တ 0 J Trecegere K Ω, CGTGCACACC GCACGTGTGG E = > TGACCAGCGG ACTGGTCGCC G တ GTCGTGGAAC TCAGGCGCCC AGTCCGCGGG H æ Ö S CAGCACCTTG z 3 တ CGGTGACGGT GCCACTGCCA 2101 177

CGGGTTTAGA GCCCANATCI ഗ × ۵, CAGCAACACC AAGGTGGACA AGAAAGTTGA TCTTTCAACT (L) × TTCCACCTGT Ω > GTCGTTGTGG E Ż S TGCAACGTGA ATCACAAGCC TAGTGTTCGG × =ACGITGCACT > Z GACCTACATC CTGGATGTAG > ₽ TGGCCACCCA ACCCGTGGGT O ₽ ဗ TCTAGCAGCT AGATCGTCGA S တ CTGACACGGG GACTGTGCCC ۵. > 2201 210

ACCCTCATGA TGGGAGTACT H TCCCCCAAA ACCCAAGGAC TGGGTTCCTG ρ. AGGGGGGTTT ρ, ۵, GICTICCICT CAGAAGGAGA **.** Ç£, > CCAGCACCTG AACTCCTGGG GGGACCGTCA CCCTGGCAGT လ ρ, Ö TTGAGGACCC Ö u L GGTCGTGGAC ρ, æ Ω, CCCACCGTGC GGGTGGCACG O Ω, Ω, CTCACACATG GAGTGTGTAC O ₽  $\Xi$ TGTGACAAAA ACACTGTTTT 2301 243

GACGGCGTGG AGGTGCATAA TCCACGTATT × CTGCCGCACC Ö Ω CTGGTACGTG GACCATGCAC >-3 TCAAGTTCAA AGTTCAAGTT ſı, GAGCCACGAA GACCCTGAGG CTGGGACTCC ш ۵, CTCGGTGCTT = လ ACATGCGTGG TGGTGGACGT ACCACCTGCA Ω TGTACGCACC > O CCCTGAGGTC GGGACTCCAG > ω ۵, TCTCCCGGAC AGAGGCCTG œ တ 2401 277

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GTTCCTCATG TGCCAAGACA AAGCCGCGGG AGGAGCAGTA CAACAGCACG TACCGTGTGG TCAGCGTCCT CACCGTCCTG CACCAGGACT GGCTGAATGG CAAGGAGTAC CCGACTTACC z GTGGCAGGAC GTGGTCCTGA Ω O H GITGICGIGC AIGGCACACC AGICGCAGGA > œ ഗ z TCCTCGTCAT > O (1) Tregeeecc ρ, ACGGTTCTGT 2501 310

TGGGACGGG CCCGAGAACC ACAGGTGTAC ACCCTGCCCC TGTCCACATG GGCTCTTGG AGCCCTCCCA GCCCCCATCG AGNAAACCAT CTCCAAAGCC AAAGGGCAGC TTTCCCGTCG GAGGTTTCGG TCTTTTGGTA CGGGGGTAGC TCGGGAGGGT AAGTGCAAGG TCTCCAACAA AGAGGTTGTT TTCACGTTCC 2601

۵, w α. O ပ × ഗ ۵, K L K z 343

GCAATGGGCA CGTTACCCGT ပ CTCACCCTCT GAGTGGGAGA ы GTAGCGGCAC CATCGCCGTG æ ù AAAGGCTTCT ATCCCAGCGA TITCCGAAGA TAGGGICGCI Ω S Ω, CL. ဗ CTGCCTGGTC GACCCACCAC L O TCTCTACTGG TTCTTGGTCC AGTCGGACTG AAGAACCAGG TCAGCCTGAC u S O z AGAGATGACC Σ Сı CATCCCGGGA GTAGGGCCCT 2701 377

GTGGCAGCAG CTCACCGTGG ACAAGAGCAG rericrest α, တ GAGTGGCACC > E CTACAGCAAG GATGTCGTTC × S > CCTTCTTCCT GGAAGAAGGA ſĿ, Çe, TCCGACGGCT AGGCTGCCGA ပ Ω CGTGCTGGAC GCACGACCTG GGTGCGGAGG CCACGCCTCC ۵, Q, H AACTACAAGA TTGATGTTCT × > GCCGGAGAAC CGCCTCTTG (±) ρ, 2801

TGCGACGGCC TAAATAAGCA ATTTATTCGT TGTCTCCGGG ACAGAGGCCC GAGGCTCTGC ACAACCACTA CACGCAGAAG AGCCTCTCCC TCGGAGAGGG S H GTGCGTCTTC O **[-**TGTTGGTGAT = z CTCCGAGACG K CGTGATGCAT GCACTACGTA = Σ > TCTCATGCTC AGAGTACGAG ပ ഗ GGGAACGTCT CCCTTGCAGA > z ပ 2901 443

AATGCGGTAG TTTATCACAG CGAATAGTAG CTATTCGAAA TTACGCCATC AAATAGTGTC TAACGCTCGG TIGCCGCCGG GCGTITITIA INGITAACTC AIGITHGACA GCTIAICAIC GAIAAGCTIT ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAATTGAG TACAAACTGT SATCTCAGGG CTAGAGTCCC 3001

TIMANTIGCT AACGCAGTCA GCCACCGTGT ATGAAATCTA ACAATGCGCT CATCGTCATC CTCGGCACCG TCACCCTGGA TGCTGTAGGC ATAGGCTTGG ACGACATCCG TATCCGAACC GTAGCAGTAG GAGCCGTGGC AGTGGGACCT CCGTGGCACA TACTTTAGAT TGTTACGCGA TTGCGTCAGT AATTTAACGA 3101

\$ ACTGCCGGGC CTCTTGCGGG ATATCGTCCA TGACGGCCCG GAGAACGCCC TATAGCAGGT TTATGCCGGT 3201

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TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC CTCGTCAGTA CCGGGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT CCCTGATATC GCGACTATAG TITIAATGIA TITGIAACIA GIACGCAAGI CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA Ω Anti-VEGF Light chain TTGAAGCATC TCTATTGCTA CAAACGCGTA CITAAGIIGA AGAGGIAIGA AACCIAIICC IITAIGICIG TACIIITIAG AGIAACGACI CAACAAIAAA IICGAACGGG IÏITICIICI GTTTGCGCAT CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA CAAGCAAAA AGATAACGAT SIAT TCTTTTTATT GTTCGTTTTT EL. > Œ. ATAGTCCCTT AACGTAGATA TTGCATCTAT Σ ဟ TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC CTITICAACA GCIGICATAA AGTIGICACG GCCGAGACTI CGTAAAGAAG GCATTTCTTC ٤. Æ Signal TIR -1 GAAGAATATC CTTCTTATAG z STII GAATTATGAA CTTAATACTT × GCGTCCATCT CGAGGTAAAG AGGGTATCTA TTTTCAATTA GAAAAGTTGT TCCCATAGAT CTTGACACAC GGCGCTGTA AAAAGTTAAT TCACGTAAAA GAATTCAACT 301 101 201 401

ATCGTTGATA AATTTGACCA CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT z z ഗ CAGTCCTATA Ω 0 ACGTCGCGTT æ S GTGGTAGTGG CICCCIGICC GCCICIGIGG GCGAIAGGGI CGCTATCCCA œ Ω CGGAGACACC ပ > လ ~ GAGGGACAGG ... ഗ CAGITGACCC AGICCCCGAG TCAGGGGCTC S တ GTCAACTGGG O 501

CAAGACCCTG TOTGGATCCG AGACCTAGGC S ပ AAGAGCGAAG TTCTCGCTTC ſ. œ S GACCTCAGGG CTGGAGTCCC ۵. > ပ TCTCTCCACT AGAGGGTGA × **۔**، GAAGTGGAGG CTTCACCTCC S €--Ĺ. CGAGGCTTTC ATGACTAAAT GCTCCGAAAG TACTGATTTA >-Н J × O. ACCAGGAAAA TGGTCCTTTT ပ Q, ATCAACAGAA TAGTTGTCTT 0 0 601 9

ACAGGGTACC o GGACGTTTGG CCTGCAAACC TGTCATATCG TGGCACGGCA ACCGTGCCGT ۵, > L ATTACTGTCA ACAGTATAGC ഗ >-0 TAATGACAGT ပ AAGCGTTGAA TICGCAACTI Æ u GCCAGAAGAC CGGTCTTCTG Ω W GCAGTCTGCA CGTCAGACGT د. S CTGACCATCA GACTGGTAGT  $\leftarrow$ GGATTTCACT CCTAAAGTGA 701 3

recricter ererectee CACACGGACG ACGAAGACAA TTAGACCTTG TCAAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC CTCGTCAACT 0 CGGTAGACTA ဟ GGTAGACAGA AGTAGAAGGG (L. ACACCGACGT æ AGTTTGCTTG œ AAGGTGGAGA TTCCACCTCT 801 126

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GTCACAGAGC AGGACAGCAA TCCTGTCGTT 0 CAGTGTCTCG H CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC CCAGGAGAGT CCACCTATTG CGGGAGGTTA GCCCATTGAG GGTCCTCTCA တ (L) 0 ഗ z ပ o J A z 0 > ATGTCACCTT 3 o CICCGGITIC > × « ш GATAGGGTCT ۵, >-TGAATAACTT ACTTATTGAA ſ. z z 901 160

TCACCCATCA GGGCCTGAGC CCCGGACTCG AGTGGGTAGT ACGAGAAACA CAAAGTCTAC GCCTGCGAAG CTGCGACTCG TITCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC **>** O « × > × = × ш GGACAGCACC TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ۲ ۵ **∢** ⊻ တ ٦ ٦ CGTCGTGGGA H ဟ CCTGTCGTGG ATGTCGGAGT တ Y S  $\vdash$ 1001 193

TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGGATCT AGGCCTAACG CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA TCCGGATTGC ပ မ GTTGTCCCCT ပ œ z GTTTCTCGAA ഗ AGCGGGCAGT ρ. 1101 226

SAGCCAACGG CGGCCCGCAA AAAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA CTCGGTTGCC GCCGGGCGTT TTTATTGTT GCCGACGCGC ATCTCGAATG AACTGTGTG GCAGGTAGAA GCTTTGGAGA TATCGTCAC TGCAATGCTT 1201

CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GGCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG GGTTGTCGCC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTCG GGCTACGGTC GTAAGGACTG CTGCTATGCC GCGTTTTACT CGCAATATGG SCGTTATACC 1301

AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA GGCTCTGAAT CGACGACGC GCTAATGCAT TICTICAATA ACTICGIAGG AGCAGICATI TITCAATIAG AAAAGTIGIC GACAGIATIT CAACAGIGCC 1401

ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA 1501 TAGTCGCTTT GITITIATIT ITIAATGTAT ITGTAACTAG TACGCAAGTI CACGTAAAAA GGGTATCTAG AAITAIGAAG AAGAATATCG CAITICTTCI

N A Y A E V Q L V E S G
Anti-VEGF Heavy Chain
FIG. 3B

ACGIAGAIAC AAGCAAAAA GAIAACGAIG ITIGCGCAIG CGACICCAAG ICGACCACCI CAGACCGCCA CCGGACCACG ICGGICCCCC GAGIGAGGCA

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1601 TGCATCTATG TICGITITIT CIATIGCTAC AAACGCGTAC GCIGAGGITC AGCIGGIGGA GICIGGCGGI GGCCIGGIGC AGCCAGGGGG CICACICCGI

STII Signal TIR-1

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TGGATTAACA ACCTAATIGE ATGGGTTGGA TACCCAACCT ပ > 3 GGTCCGTCAG GCCCCGGGTA AGGGCCTGGA CGGGCCCAT TCCCGGACCT W ۔۔ ပ ပ ۵. CCAGGCAGTC 0 œ > CTACGACTIC ACGCACTACG GTATGAACTG CATACTTGAC z Z GATGCTGAAG TGCGTGATGC ပ x ← G. Ω >-TIGICCIGIG CAGCITICIGG GTCGAAGACC S AACAGGACAC

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TGAACAGCCT ACTTGTCGGA \_ ഗ Z. TACCTGCAGA ATGGACGTCT 0 \_\_ AAGCACAGCA TTCGTGTCGT  $\vdash$ S ACACCTCCAA TGTGGAGGTT × S ⋳ TTTTCTTTAG AAAAGAAATC Ω د. ဟ AGCAAAGTGA TCGTTTCACT  $\leftarrow$ Œ. 0< TAMAGITIC TATGCTGCGG ATTTCAAACG × Œ ATACGACGCC Ω 4 X X ACTIGGCTGG TGAACCGACC  $\vdash$ w CCTATACCGG GGATATGGCC ပ ⊱ 1801 7

AACCCTGGTC TTGGGACCAG GGGGTCAAGG CCCAGTTCC ပ 0 G CCGTACTATT ACGCCACGAG CCACTGGTAT TTCGACGTCT AAGCTGCAGA > Ω GGTGACCATA >-3 = TGCCGTGCTC H ပ GGCATGATAA >->-GACACTGCCG TCTATTACTG TGCAAAGTAC ACGITICATG >-× æ AGATAATGAC C >->-CTGTGACGGC æ ۲ Ω GCCCCCTGAG CGCGCGACTC Œ ø. 1901 110

TGCCTGGTCA ACGGACCAGT \_ CCGGGACCCG GCCCTGGGC ပ .. GGGCCACAGC CCCCGTGTCG ~ ₽ ပ AGCACCTCTG TCGTGGAGAC ပ S F CTCCTCCAAG GAGGAGGTTC × ഗ S GGGACCGTGG CCCTGGCACC ۵. æ ۔. TCGGTCTTCC AGCCAGAAGG ۵. Œ. > CAAGGGCCCA GTTCCCGGGT ۵. G × CGGCCTCCAC GCCGGAGGTG S æ TGCCAGAGGA ACCGICTCCI S > €-2001 143

CAGGACTCTA GTCCTGAGAT >-ပ CTACAGTCCT GATGTCAGGA 0 CCCGGCTGTC GGGCCGACAG > æ م ACGTGTGGAA TGCACACCTT H **=** ACCAGCGGCG TGGTCGCCGC ပ S AGGCGCCCTG TCCCCCGGAC u ~ ပ CGTGGAACTC GCACCTTGAG ഗ z 3 GTGACGGTGT CACTGCCACA S > **(**--CCCCGAACCG GGGCTTGGC ш Q, AGGACTACTT TCCTGATGAA Ω 2101 177

GGTGGACAAG CCACCTGTTC × Ω > GCAACACCAA CGTTGTGGTT  $\vdash$ z CCTACATCTG CAACGTGAAT CACAAGCCCA GTGTTCGGGT ۵, × × GTTGCACTTA z > z GGATGTAGAC U >-GGCACCCAGA CCGTGGGTCT 0 TAGCAGCTTG ATCGTCGAAC J S ဟ CIGIGCCCIC GACACGGGAG م AGCGTGGTGA TCGCACCACT > > CTCCCTCAGC SAGGGAGTCG ഗ S 2201 210

CCCCCAAAC GGGGTTTTG ۵. CITCCTCTTC GAAGGAGAAG £4. \_ CTGGCAGTCA GACCGTCAGT S ۵. GAGGACCCCC CTCCTGGGG ပ ے AGCACCTGAA TCGTCGACTT (L) م æ GTGGCACGGG CACCGIGCCC Ω, U ۵. ACTGITITGA GIGIGIACGG CACACATGCC ۵. ပ H TGACAAAACT • × Ω GGTTTAGAAC CCANATCTTG O ഗ TTTCAACTCG AAAGTTGAGC ω > × 2301 243

GGTACGTGGA CCATGCACCT TTCAAGTTGA AAGTTCAACT 3 z Œ. CCCTGAGGTC GGGACTCCAG w GCCACGAAGA CGGTGCTTCT w I GTGCACGTGA CACCTGCACT > 0 ATGCGTGGTG TACGCACCAC > > U CTGAGGTCAC GACTCCAGTG > ധ GGAGTACTAG AGGGCCTGGG TCCCGGACCC œ CCTCATGATC Σ .. CCAAGGACAC SGTTCCTGTG Ω 2401 277

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CCAGGACTGG GGTCCTGACC CGAGAACCAC GCTCTTGGTG 0 TCGCCGTGGA AGCGGCACCT w 3 ۵. > ω ~ 0 CCCTCCTCCA CCCAGCGACA AGGCAGCCC TCCCGTCGG GCCAGGACGT GGGTCGCTGT ۵. Ω ے 0 S CCGTGTGGTC AGCGTCCTCA CCAAGCCAA TCCGAAGATA TITIGGIAGA GGIITICGGII TCGCAGGAGT GCCTGGTCAA AGGCTTCTAT >-\_ ~ Ce. > × ၒ CCCCATCGAG AAAACCATCT GGCACACCAG CGGACCAGTT × > **-**> > H \_ œ GCCGCGGGAG GAGCAGTACA ACAGCACGTA CACGITCCAG AGGITGIIIC GGGAGGGICG GGGGIAGCTC TCGGACTGGA TGTCGTGCAT AGCCTGACCT > ω ←  $\vdash$ **-**\_ ഗ ۵ ഗ CTCGTCATGT TCCCGGGAAG AGATGACCAA GAACCAGGTC CCCTCCCAGC CTTGGTCCAG 4 > >-۵. 0 0 ے z GTGCAAGGTC TCCAACAAAG CGCCCCTC TCTACTGGTT × ധ × œ z Σ م CGCCTGGAG GTGCATAATG CCAAGACAAA AGGCCCCTTC GGTTCTCTTT u > ú × **~** U CACGTATTAC CTGAATGGCA AGGAGTACAA TCCTCATGTT CCTGCCCCCA GGACGGGGT Δ, z >-۵. · = ω \_ GACTTACCGT SCCCCACCTC AGGTGTACAC TCCACATGTG  $\simeq$ ω ၒ > z ပ ... 2501 310 2601 343 2701 377

CACCGTGGAC GTGGCACCTG CCTCTCCCTG TCTCCGGGTA AGAGGCCCAT ပ > ۵. ഗ ACAGCAAGCT TGTCGTTCGA GGAGAGGGAC × ഗ ഗ CGCAGAAGAG TTCTTCCTCT AAGAAGGAGA GCGTCTTCTC >-ب **×** Œ. 0 GCTGCCGAGG GAACGICTIC ICAIGCICCG IGAIGCAIGA GCCICIGCAC AACCACIACA TTGGTGATGT CGACGGCTCC S **>**-ပ =Ω z TGCTGGACTC CCGAGACGTG TGCGGAGGGC ACGACCTGAG S × Ω د. • ACCCCTCCCG ACTACGTACT w ۵, I ۵. Σ AGTACGAGGC CTACAAGACC GATGTTCTGG  $\leftarrow$ ഗ × U >-ഗ CGGAGAACAA GCCTCTTGTT CTTGCAGAAG z Ç. z > ω z AATGGGCAGC TTACCCGTCG GCCACCAGGG CCGTCGTCCC O O ပ္ O AAGAGCAGGT GTGGGAGAGC CACCCTCTCG TTCTCGTCCA S  $\alpha$ ω ഗ 3 2901 2801 410 443

TTATCATCGA TAAGCTTTAA ATTCGARATT AATAGTAGCT GTTTGACAGC CAAAAATAA CAATTGAGTA CAAACTGTCG GTTAACTCAT GITITITATI 000000000 GCTGCCGGGA TCTCAGGGAT TGCGAGCCAA CGGCGGCCCG CGACGGCCCT AGAGTCCCTA ACGCTCGGTT AATAAGCATG **TATTCGTAC** 0 3001 477 TGCGGTAGTT TATCACAGTT AAATTGCTAA CGCAGTCAGG CACCGTGTAT GAAATCTAAC AATGCGCTCA TCGTCATCCT CGGCACCGTC ACCCTGGATG ACGCCATCAA ATAGTGTCAA TITAACGATI GCGTCAGTCC GTGGCACATA CTTTAGATIG ITACGCGAGT AGCAGTAGGA GGCGTGGCAG TGGGACCTAC Start Tet Resistance Coding Sequence 3101

CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCCT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT SACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCGGA GAACGCCCTA TAGCAGGTAA GGCTGTCGTA GCGGTCAGTG ATACCGCACG ACGATCGCGA 3201

Inventor: REILLY ET AL. Docket No.: 11669.195USU1

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TTCGAACGGG

CAACAATAAA

CAGGTAGAGG GTTGATTGAT CAACTAACTA ACCAACAGCG TGGTTGTCGC CGCGTTTTAC GCGCAAAATG AGCGTTATAC TCGCAATATG GACGTTACGA CTGCAATGCT ATTATCGTCA TAATAGCAGT AGCTTTGGAG TCGAAACCTC GCGTCCATCT CTTGACACAC

GAATTCAACT TCTCCATACT TIGGATAAGG AAATACAGAC AIGAAAAATC TCATIGCIGA GTIGITAITT AAGCTIGCCC AAAAAGAAGA AGAGICGAAT

AACCTATTCC TITATGTCTG TACTITITAG AGTAACGACT

AGAGGTATGA

CTTAAGTTGA

CGCAGGTAGA

101

CTCGTCAGTA GAGCAGTCAT TTGAAGCATC AACTTCGTAG AAAGAAGTTA TTTCTTCAAT GCGATTACGT CGCTAATGCA GAGCTGCTGC CTCGACGACG GCATTCCTGA CGACGATACG CGTAAGGACT GCTGCTATGC CCCGATGCCA GGGCTACGGT CGAGGTAAAG SCCGCGACAT GCTCCATTIC GGCGCTGTA 201

CATGCGTTCA TTTGTAACTA AAACATTGAT TTTTAATGTA TATCAGCGAA ACAAAATAA AAAATTACAT TGTTTTTTT ATAGTCGCTT GCCGAGACTT CGGCTCTGAA AGTIGICACG TCAACAGTGC GCTGTCATAA CGACAGTATT CTTTTCAACA GAAAAGTTGT AAAAGTTAAT TTTTCAATTA 301

CGCTGATATC GCGACTATAG 4 CAAACGCGTA GTTTGCGCAT æ z TCTATTGCTA AGATAACGAT GTTCGTTTTT CAAGCAAAAA Œ, > Cz. TTGCATCTAT AACGTAGATA လ CGTAAAGAAG GCATTTCTTC Cz, A CTTCTTATAG GAAGAATATC Z GAATTATGAA CTTAATACTT AGGGTATCTA TCCCATAGAT TCACGTAAAA AGTGCATTTT

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AATTTGACCA TTAAACTGGT TAGCAACTAT ATCGTTGATA CAGTCCTATA GTCAGGATAT TGCAGCGCAA ACGTCGCGTT CACCATCACC GTGGTAGTGG GCGATAGGGT CGCTATCCCA GCCTCTGTGG CGGAGACACC GAGGGACAGG CTCCCTGTCC AGTCCCCGAG TCAGGGGCTC GTCAACTGGG 501

GTTCTGGGAC CAAGACCCTG တ TCTGGATCCG AGACCTAGGC S G Trerective AAGAGCGAAG Œ, œ ഗ CTGGAGTCCC GACCTCAGGG > Ö TCTCTCCACT AGAGGGGGA =J တ CTTCACCTCC GAAGTGGAGG S ۲ Ĺ, TACTGATTTA ATGACTAAAT Н J GCTCCGAAAG CGAGGCTTTC × a, æ ACCAGGAAAA TGGTCCTTTT × G ATCAACAGAA TAGTTGTCTT O O 601 9

TGTCCCATGG ACAGGGTACC ပ O GGACGTTTGG CCTGCAAACC ACCGIGCCGI TGGCACGGCA ۵, > ACAGTATAGC TGTCATATCG S >-O ATTACTGTCA TAATGACAGT O TTCGCAACTT AAGCGTTGAA ₽ ⋖ GCCAGAAGAC CGGTCTTCTG Ω ω Ω, GCAGTCTGCA CGTCAGACGT O u S CTGACCATCA GACTGGTAGT ₽ CCTAAAGTGA GGATTTCACT ⋳ Cz. Ω 701 8

H CACACGGACG GTGTGCCTGC C TGCTTCTGTT ACGAAGACAA S Ø GAGCAGTIGA AATCIGGAAC TTAGACCTTG G တ CTCGTCAACT **.** O Œ CGGTAGACTA GCCATCTGAT Ω တ Ω, TCATCTTCCC AGTAGAAGGG Œ, Н CCATCTGTCT GGTAGACAGA > ഗ TGTGGCTGCA ACACCGACGT æ > TCAAACGAAC AGTTTGCTTG œ AAGGTGGAGA w > × 801 126

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TCCTGTCGTT CAGTGTCTCG w GGTCCTCTCA ω O GCCCATTGAG z G CGGGAGGTTA O CCACCTATTG Ω > CICCGGITIC AIGICACCIT 3 o 4 ω GATAGGGTCT œ ۵, ACTIATIGAA

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901 TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA

GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCCTGAGC CCCGGACTCG GTTTCAGATG CGGACGCTTC AGTGGGTAGT = > ω U **⊁** > × CIGCGACTCG TITCGTCTGA IGCTCTITGT = × Œ Ω A X လ ... ₽ CCTGTCGTGG ATGTCGGAGT CGTCGTGGGA GGACAGCACC TACAGCCTCA GCAGCACCCT H ⊱ တ ... S တ Ω 1001 193

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG CICACAAITA AITTAGGAGA IGCGGCCIGC GIAGCACCGC ICGAGCCAIG GGCCCCIAGA ICCGGAITGC ပ မ GTTGTCCCCT ල 2 z GTTTCTCGAA Ce, တ × AGCGGGCAGT > 226

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CTCGGTTGCC GCCGGGCGTT TTTATTGTT GCCGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT GAGCCAACGG CGGCCCGCAA AAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACGC CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA 1201

CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GGCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG GCGTTATACC GCGTTTTACT GGTTGTCGCC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTCG GGCTACGGTC GTAAGGACTG CTGCTATGCC 1301

1401 AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA ICGACGACGC GCTAATGCAT TICTICAATA ACTICGTAGG AGCAGTCATT TITCAATTAG AAAAGTIGIC GACAGTATTI CAACAGIGCC GGCTCTGAAT

ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATACTTC TTGTTATAGC GTAAAGAAGA 1501 TAGTCGCTTT GTTTTTATTT TTTAATGTAT TTGTAACTAG TACGCAAGTT CACGTAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT .a K I N X ×

start heavy chain N O I A

1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGCGTAC GCTGAGGTTC AGCTGGTGGA GTCTGGCGGT GGCCTGGTGC AGGCAGGGGG CTCACTCCGT

CGACTCCAAG TCGACCACCT

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ACGTAGATAC AAGCAAAAA

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Inventor: REILLY ET AL. Docket No.: 11669.195USU1

Docket No.: 11609.1950S01

Title: METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION

Serial No.: 10/697

TGGATTAACA ACCTAATTGT ATGGGTTGGA TACCCAACCT Ö > 3 GCCCCGGGTA AGGGCCTGGA TCCCGGACCT J CGGGGCCCAT G ρ, GGTCCGTCAG CCAGGCAGTC 0 æ > CIATACCITC ACCAACIAIG GIATAAACIG CATATTTGAC z TGGTTGATAC >-Z GATATGGAAG E CAGCTTCTGG GTCGAAGACC တ TIGICCIGIG AACAGGACAC O တ u 43

ACTIGICGGA TGAACAGCCI TACCTGCAGA ATGGACGTCT Σ O u AAGCACAGCA TTCGTGTCGT æ H ഗ TITICITIAG ACACCICCAA TGTGGAGGTT × တ ₽ AAAAGAAATC L S AGCAAAGTGA TCGTTTCACT ₽ Ĺz, œ TAAAGTTTGC ATTTCAAACG × Çe. ATACGACGCC TATGCTGCGG A Ø ACTTGGCTGG TGAACCGACC H Ω, ഥ CCTATACCGG GGATATGGCC 1801 77

GGGTCAAGGA CCCAGTTCCT ပ 0 ဗ TCGACGTCTG AGCTGCAGAC > Ω CACTGGTATT GTGACCATAA Ç, >-3 GCGGAAGAGC CGCCTTCTCG ഗ × œ TACACTTGCT ATGTGAACGA ω z > GGCGTGATAA CCGCACTATT > =۵, TGCAAAGTAC ACGITTCATG > × K AGATAATGAC TCTATTACTG O >-> CTGTGACGGC GACACTGCCG æ ₽ GCGCGCTGAG CGCGCGACTC ξij K œ 1901 110

CGGGACCCGA GCCCTGGGCT ပ GGCCACAGCG Cécerercec K E+ GCACCTCTGG CGTGGAGACC O S ₽-4 TCCTCCAAGA AGGAGGTTCT S × S CCTGGCACCC GGACCGTGGG ρ, æ H CGGTCTTCCC GCCAGAAGGG Ω Ĺz, > TTCCCGGGTA AAGGCCCCAT ρ. ပ GGCCTCCACC CCGGAGGTGG ₽ တ 4 GGCAGAGGAG CCGTCTCCTC S S > ACCCTGGTCA TGGGACCAGT > H ₽ 2001 143

TACAGICCIC ATGTCAGGAG ഗ O CCGCCTGTCC GGCCGACAGG > 4 GCACACCTTC CGTGTGGAAG Œ, ₽ I CCAGCGGCGT GGTCGCCGCA > O S GGCGCCCTGA CCGCGGGACT u æ GTGGAACTCA CACCTTGAGT တ z 3 TGACGGTGTC ACTGCCACAG S > CCCGAACCGG GGCTTGGCC Δ, ш GGACTACTTC CCTGATGAAG Œ, >-GCCTGGTCAA CGGACCAGIT > u 2101 177

CAACACCAAG GTTGTGGTTC × z ACAAGCCCAG Terreggic တ ۵, AACGTGAATC TTGCACTTAG z > z CTACATCTGC GATGTAGACG O >-GCACCCAGAC CGTGGGTCTG ₽ O ₽ AGCAGCTTGG TCGTCGAACC G ᆸ S S TGTGCCCTCT ACACGGGAGA S ۵, > GCGTGGTGAC CGCACCACTG ₽ > > TCCCTCAGCA AGGGAGTCGT S ഗ AGGACTCTAC TCCTGAGATG > ... G 2201 210

TICCICITIC AAGGAGAAGG ACCGTCAGTC TGGCAGTCAG ഗ TCCTGGGGGG AGGACCCCCC Ö Ö u GCACCTGAAC CGTGGACTTG Œ ρ, Ä ACCGIGCCCA TGGCACGGGT p, O Δ, ACACATGCCC TGTGTACGGG C ₽ GACAAAACTC CTGTTTTGAG I × Ω CAAATCTTGT GTTTAGAACA O တ × AAGTTGAGCC TTCAACTCGG W > GTGGACAAGA CACCTGTTCT × Ω > 2301 243

AGTTCAACTG TCAAGTTGAC 3 Œ. CCTGAGGTCA GGACTCCAGT Œ CCACGAAGAC GETGCTTCTG ш × recereeree recacereae ACCTGCACTC > Ω ACGCACCACC > > TGAGGTCACA ACTCCAGTGT > ω CCCGGACCCC GGGCCTGGGG Ω, œ CTCATGATCT GAGTACTAGA Σ CAAGGACACC GTTCCTGTGG Ω CCCCAAAACC GGGTTTTGG 2401 277

FIG. 4C

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CGTCCTGCAC GCAGGACGTG GTACGIGGAC GGCGIGGAGG IGCAIAAIGC CAAGACAAAG CCGCGGGAGG AGCAGIACAA CAGCACGIAC CGIGIGGICA GCGICCICAC gregreate geacaceagt cecagagte **ب** လ > > ۲ တ CCGCACCTCC ACGTATTACG GITCTGTTTC GGCGCCCTCC TCGTCATGTT >o Œ œ × E × z = ш > ဗ CATGCACCTG > 2501 310

CAAAGCCAAA GGGCAGCCCC CCCGTCGGGG Ω, 0 GTTTCGGTTT × æ × cereceage cecaregaga AAACCATETE TTTGGTAGAG S ₽ GGGTAGCTCT w **—** Δ, GGAGGGTCGG æ ρ, L GGAGTACAAG TGCAAGGTCT CCAACAAAGC GGTTGTTTCG Ø × z ACGITCCAGA > × CCTCATGTTC × >-Сı TGAATGGCAA ACTTACCGTT ဇာ z 2601 CAGGACTGGC GTCCTGACCG ø 343

GGTCGCTGTA CCAGCGACAT GGCTTCTATC CCGAAGATAG (z. ပ GATGACCAAG AACCAGGTCA GCCTGACCTG CCTGGTCAAA GGACCAGTTT × > .\_ CGGACTGGAC ပ ۲ ᆸ TTGGTCCAGT S > O z CTACTGGTTC × ₽ Σ CCCGGGAAGA GGGCCCTTCT (L) ш œ CTGCCCCCAT GACGGGGGTA S Ω, ۵. J CCACATGTGG GGTGTACACC H >-> GAGAACCACA CTCTTGGTGT O ۵, Œ 2701 377

TCTTCCTCTA CAGCAAGCTC GTCGTTCGAG u × S CTGCCGAGGA AGAAGGAGAT .\_ CGCCTCCCGT GCTGGACTCC GACGGCTCCT တ ပ CGACCTGAGG တ Ω ... GCGGAGGGCA > Δ, ۵, TACAAGACCA ATGTTCTGGT ۲ × CCTCTTGTTG GGAGAACAAC z z (L) TGGGAGAGCA ATGGGCAGCC TACCCGTCGG 0 ပ ACCCTCTCGT S ш 3 CGCCGTGGAG GCGCACCTC Œ > 2801 410

GAGAGGGACA S CTCTCCCTGT ... ഗ CGTCTTCTCG GCAGAAGAGC S × ō GCTCTGCACA ACCACTACAC TGGTGATGTG ₽ >-= CGAGACGTGT Z = ... A GATGCATGAG CTACGTACTC Œ I Σ TTGCAGAAGA GTACGAGGCA CATGCTCCGT > တ ပ AACGTCTTCT S Ce. > GCAGCAGGGG CGTCGTCCCC G O O TCTCGTCCAC AGAGCAGGTG 3 α; ഗ TGGCACCTGT ACCGTGGACA Ω > ⊢ 2901 443

TATCATCGAT ATAGTAGCTA TTTGACAGCT GGCGCCCCC AAAAATAAC AATTGAGTAC AAACTGTCGA CCCCCCCCCC TITITATIC ITAACTCAIG GAGTCCCTAA CGCTCGGTTG CTCAGGGATT GCGAGCCAAC CTGCCGGGAT GACGCCCTA TATTCGTACG ATAAGCATGC 0 CTCCGGGTAA GAGGCCCATT O Δ. 3001 477

^lambda terminator

GOGGIAGITI ATCACAGITA AATTGCIAAC GCAGICAGGC ACCGIGIAIG AAAICIAACA AIGCGCICAI CGICAICCIC GGCACCGICA CCGTGGCAGT TGGCACATAC TITAGATIGI TACGCGAGIA GCAGTAGGAG CGTCAGTCCG TTAACGATTG TAGTGTCAAT CGCCATCAAA AAGCTTTAAT **LTCGAAATTA** 3101

36GACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CGGCCCGGAG AACGC CCCTGGATGC TGTAGGCATA GCCTTGGTTA TGCCGGTACT GCCGGGCCTC

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TAGCTACITIA AGTACGACAC CACAGIACCA GCCACIAGCG GICCCACGGC IGCGCGIAGA GCIGACGIGC CACGIGGITA CGAAGACCGC AGICCGICGG 101 ATCGGAAGCT GTGGTATGGC TGTGCAGGTC GTAAATCACT GCATAATTCG TGTCGCTCAA GGCGCACTCC CGTTCTGGAT AATGTTTTT GCGCCGACAT TAGCCTTCGA CACCATACCG ACACGTCCAG CATTTAGTGA CGTATTAAGC ACAGCGAGTT CCGCGTGAGG GCAAGACCTA TTACAAAAA CGCGGCTGTA

ATCGATGAAT TCATGCTGTG GTGTCATGGT CGGTGATCGC CAGGGTGCCG ACGCGCATCT CGACTGCACG GTGCACCAAT GCTTCTGGCG TCAGGCAGCC

ATTCGAATCC CCTATTGTTA CTGGCAAATA TICTGAAATG AGCTGTTGAC AATTAATCAT CGAACTAGTT TAATGTGTGG AATTGTGAGC GGATAACAAT GACCETTTAT AAGACTTTAC TCGACAACTG TTAATTAGTA GCTTGATCAA ATTACACACC TTAACACTCG CATAACGGTT STATTGCCAA 201

GCTGCTGAAG CGACGACTTC (ci) ø TGCATGCACC AATCACTTTT TTAGTGAAAA ACGTACGTGG æ **:** GCCGTTGCCC CGGCAACGGG ⋖ CGCTGCTGGC GACCACAATG CTGGTGTTAC ₽ ₽ GCGACGACCG . TTTAAAGTAA AAATTTCATT × GAAGATTTAT GAAATCACTG CITCIAAAIA CITIAGIGAC ^fkpA start ഗ 301 ATTCTAGAGG TAAGATCTCC

GTTACATGGA CAATGTACCT ACTGGGTGCC TCGCTGGGTC AGCGACCCAG Ö TGACCCACGG æ Ö H CAAAAATGAC GATCAGAAAT CAGCTTATGC GTCGAATACG 4 >-Þ CTAGTCTTTA × O GITTITACIG Ω z × GCTGACAGCA AAGCAGCGTT TTCGTCGCAA Çz. ø Ø CGACTGTCGT ഗ Ω K TGCTACAGCT ACGATGTCGA æ E→ 4 CTGCAAAACC GACGTTTTGG × æ 401 23

CAAACTCTCC GTTTGAGAGG GATGCATTTG CTGATAAGAG GACTATTCTC Ω CTACGTAAAC 4 TGGTGTTCAG ACCACAAGTC O > Ö GATAAAGATC AGCTGATCGC TCGACTAGCG н ᆸ CTATTTCTAG O Ω × CATCAAACTG GTAGTTTGAC H × AAAAACTGGG TTTTTGACCC J × AAAGAACAAG TTTCTTGTTC O (x) AAACTCTCTA TTTGAGAGAT ഗ z 501 62

TTCTGCTCAG GCGAAGATGG AAAAAGACGC GGCTGATAAC GAAGCAAAAG CTTCGTTTTC CCGACTATTG Ω 4 TTTTTCTGCG Ω CGCTTCTACC Σ × AAGACGAGTC O A ഗ Tresagere ecercaagre CGCACTTCAG × AAGCTTCGAG Ø 山 TCTACAAGCA AGATGTTCGT 4 O 口 GACCAAGAGA TCGAACAGAC AGCTTGTCTG 0 Œ CIGGITCICI (±) 601 95

GCCGGTAAAG GCGAAGCACC CGCTTCGTGG CGGCCALTIC ဗ GGTAGTAGAA CCATCATCTT TCAACTGGTC TGGTTTATCA CTTTTGGAGA AGTTGACCAG ACCAAATAGT O >-> ᆸ Ö GAAAACCTCT လ H × TTTGCCAAAG AGAAAGGTGT TCTTTCCACA O × AAACGGTTTC × 4 GGCGCTCTTT CCGCGAGAAA [1] œ GTAAAGAGTA CATTTCTCAT G 701 129

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AGAACTGGCT TACGGCAAAG AAGAAAGGCA ATGCCGTTTC TTCTTTCCGI GATGCAAAGC CGGAAGCTGA cracerrace eccraceaer œ × æ Cz, O S CGACAACTCT TACACCGGTG GTGAACCGCT CACTTGGCGA TCTTGACCGA Δ, .\_ 臼 Ω GCTGTTGAGA ATGTGGGCAC AGGCGGTAAG ATCAAACTGG TTATTCCACC TGACGTAGAG CTGCTGGATG TGAAACCAGC GCCGAAGGCT TAGITIGACC AATAAGGIGG ဗ CGGCTTCCGA Ω, æ œ ρ, × н ρ, GACGACCTAC ACTITIGGTCG ഗ H Δ, z × Ω GAAAGACAGC GATACTGTTG TAGTGAACTA CAAAGGTACG CTGATCGACG GTAAAGAGTT CATTTCTCAA TCCGCCATTC Ω Œ ဗ H Ö CTATGACAAC ATCACTTGAT GTTTCCATGC GACTAGCTGC TTGGACAGAA GGTCTGAAGA ACATCAAGAA ACTGCATCTC TGTAGTTCTT Ω × > Н Ω CCAGACTTCT GGGGATCCCA CCGAATTCTA CCCTGGTGTT GGCTTAAGAT GGGACCACAA E × > ဗ n u ¥ AACCTGTCTT 四 လ z E z 3 GACCTGCCAC AATAGGGCCC CTGGACGGTG TTATCCCGGG CCCCTAGGGT O ρ, > ρ. H CTITCIGICG CGGGTGTTCC GCCCACAAGG တ G > Ω r D Ö × 801 901 162 195 1001 229

FIG. 51

NheI

TGCGAAAGCC GCAGATTCTG CTAAAAAATA AAAGCTAGC

CGTCTAAGAC GATTTTTAT TTTCGATCG

ACGCTTTCGG

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AAAAAGAAGA AGAGTCGAAT TCTCAGCTTA TITITICITCE AAGCTTGCCC CAACAATAAA TTCGAACGGG GITGITATIT TCATTGCTGA AGAGGTATGA AACCTATTCC TITATGTCTG TACTTTTAG AGTAACGACT TTGGATAAGG AAATACAGAC ATGAAAATC TCTCCATACT CTTAAGTTGA GAATTCAACT ECORI CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG CITGACACAC GCGICCAICI ICGAAACCIC IAAIAGCAGI GACGIIACGA AGCGIIAIAC CGCGIIIIIAC IGGIIGICGC CAACIAACIA GICCAICICC GAACTGTGTG 101

GGCCCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA GCTCCATTIC GGGCTACGGT CGTAAGGACT GCTGCTAIGC CTCGACGACG CGCTAAIGCA ITTCTICAAT AACITCGIAG GAGCAGICAI CCCCCCACAT 201

CATGCGTTCA TITGIAACTA GIACGCAAGI AAACATTGAT TTTTAATGTA TCAACAGIGC CGGCTCTGAA IATCAGCGAA ACAAAAATAA AAAATTACAT TGTTTTTATT ATAGTCGCTT GCTGTCATAA AGTTGTCACG GCCGAGACTT CGACAGTATT CTTTTCAACA GAAAAGTTGT AAAAGTTAAT TTTTCAATTA 301

CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG GITCGITIII ICIAIIGCIA CAAACGCGIA CGCIGAIAIC anti-TF|light chain^ æ S > Œ. TTGCATCTAT TITCTIAIAG CGIAAAGAAG AACGIAGAIA တ K AGGGTATCTA GAATTATGAA AAAGAATATC GCATTTCTTC STII signal TIR Œ z z start TCCCATAGAT CTTAATACTT TCACGTAAAA AGTGCATTTT 401

GTCGCGACAT CAAGAGCTAT CTGAACTGGT GACTTGACCA 3 z GTTCTCGATA S CAGCGCTGTA Ω œ CACCATCACC TGCAGAGCCA ACGTCTCGGT œ GTGGTAGTGG H Н H CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CGCTATCCCA œ Ω CGGAGACACC > ഗ GAGGGACAGG ഗ ... ഗ AGTCCCCGAG TCAGGGGCTC တ Ω, 501 CAGATGACCC GTCTACTGGG Σ O 26

TCTGGATCCG GTTCTGGGAC CAAGACCCTG ဗ AAGAGCGAAG AGAĆCTAGGC ഗ TTCTCGCTTC Œ, œ ഗ CTATGCTACT AGTCTCGCTG AAGGAGTCCC TCAGAGCGAC TTCCTCAGGG Q, > ဗ Œ æ ... S GATACGATGA ø >-GCTCCGAAAG TACTGATTTA CGAGGCTTTC ATGACTAAAT Н H × ۵, æ ACCAGGAAAA TGGTCCTTTT × ပ Q, 601 ATCAACAGAA TAGTTGTCTT O O 09

ACAGGGTACC TGTCCCATGG ပ ď GAGICICCAI GGACAITIGG CCTGTAAACC ပ [z, ۲ CTCAGAGGTA 3 တ Œ TTCCCAACTT ATTACTGTCT TCAGCACGGA AGTCGTGCCT ပ I o TAATGACAGA U > AAGCGTTGAA E E CTGACCATCA GCAGTCTGCA GCCAGAAGAC CGGTCTTCTG Ω w م CGTCAGACGT ᆸ ഗ GACTGGTAGT တ H GGATTACACT CCTAATGTGA E Ω 701 8

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GIGIGCCIGC CACACGGACG .\_ O TTAGACCTTG ACGAAGACAA TCATCTICCC GCCATCTGAT GAGCAGTIGA AATCTGGAAC TGCTTCTGTT ഗ K H ဗ ഗ CTCGTCAACT ... O (LI) CGGTAGACTA Ω တ Ω, GGTAGACAGA AGTAGAAGGG Ω, Œ н TGTGGCTGCA CCATCTGTCT > ഗ Д ACACCGACGT Ø Ø, > 801 AAGGTGGAGA TCAAACGAAC AGTTTGCTTG E œ × TTCCACCTCT வ > ×

AGGACAGCAA TCCTGTCGTT × ഗ Q GTCACAGAGC CAGTGTCTCG O ш <u>ب</u> ح CCAGGAGAGT GGTCCTCTCA တ ш o CGGGTAACTC GCCCATTGAG ഗ z Ö GCCCTCCAAT CGGGAGGTTA O A L GGTGGATAAC CCACCTATTG z Ω > ATGTCACCTT GAGGCCAAAG TACAGTGGAA × 3 o CTCCGGTTTC × **д** Э CTATCCCAGA GATAGGGTCT œ Δ, >4 TGAATAACTT ACTTATTGAA z z 901 160

GGGCCTGAGC CCCGGACTCG တ G TCACCCATCA AGTGGGTAGT = AAAGCAGACT ACGAGAAACA CAAAGTCTAC GCCTGCGAAG CGGACGCTTC (±1 U GTTTCAGATG > > × TGCTCTTTGT Ξ × [L] TTTCGTCTGA Ω GACGCTGAGC CTGCGACTCG လ u E GCAGCACCCT CGTCGTGGGA ₽ ഗ TACAGCCTCA ATGTCGGAGT u တ GGACAGCACC CCTGTCGTGG ۲ တ Ω 1001 193

CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG TCCGGATTGC CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCTAGA 0 ပ ω GTTGTCCCCT œ z CAAAGAGCTT GTTTCTCGAA ſz, လ × TCGCCCGTCA AGCGGGCAGT > ഗ 1101 226

lambda to terminator^

ITITIATIGIT GCCGACGCGC ATCTCGACTG CACGGTGCAC CAATGCTTCT GGCGTCAGGC AGCCATCGGA AGCTGTGGTA AAAATAACAA CGGCTGCGCG TAGAGCTGAC GTGCCACGTG GTTACGAAGA CCGCAGTCCG TCGGTAGCCT TCGACACCAT GCCGGGCGTT CGGCCCGCAA CTCGGTTGCC SAGCCAACGG 1201

ACATCATAAC GGTTCTGGCA CCAAGACCGT TGTAGTATTG GGTCGTAAAT CACTGCATAA TTCGTGTCGC TCAAGGCGCA CTCCCGTTCT GGATAATGTT TTTTGCGCCG CCAGCATTTA GTGACGTATT AAGCACAGCG AGTTCCGCGT GAGGGCAAGA CCTATTACAA AAAACGCGGC TGGCTGTGCA ACCGACACGT 1301

TAGGATCTAG AATTATGAAG TTAATACTTC Σ CTCGCCTATT GTTAATTCGA ATCCTAGATC GTGGAATTGT GAGCGGATAA CAATTAAGCT ACTGITAATT AGTAGCITGA TCAAATTACA CACCITAACA TGACAATTAA TCATCGAACT AGTTTAATGT TTACTCGACA AATGAGCTGT AATATTCTGA TTATAAGACT 1401

Start STII signal TIR

0 GCCTGGTGC CCGGACCACG ... TITGICITIT CIAIAGCIAC AAACGCGIAC GCIGAGGIIC AGCIGGIGGA GICIGGCGGI TCGACCACCT CAGACCGCCA G ^anti-TF heavy chain [1] > ᆸ CGACTCCAAG O > ш Æ TTTGCGCATG >æ z GATATCGATG æ н ACGGAGATAC AAACAGAAAA ഗ Œ, > TGCCTCTATG Σ ഗ 4 GCAAGGATGA CGTTCCTACT H J G, 1501 AAGAATATTG TTCTTATAAC z ×

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CTCACTCCGT TIGTCCTGTG CAGCTTCTGG CTTCAATATT AAGGAGTACT ACATGCACTG GGTCCGTCAG GCCCGGGTA AGGGCCTGGA TCCCGGACCT ... CGGGGCCCAT G CCAGGCAGTC 0 œ > TGTACGTGAC Ξ TTCCTCATGA Œ GAAGTTATAA z [z, GTCGAAGACC တ AACAGGACAC ပ GAGTGAGGCA œ . ഗ 1601 AGCCAGGGG regerecee G 37

AAACACAGCA TTTGTGTCGI CCGTGCCACT ATAAGCGCTG ACAATTCCAA TGTTAAGGTT S TATTCGCGAC 4 ഗ GCACGGTGA ~ œ CAACACGATC TATGACCCGA AGTTCCAGGA ATACTGGGCT TCAAGGTCCT Ω O ſz, ρ, Ω GTTGTGCTAG ۲ z TTGATTGATC CAGAGCAAGG GTCTCGTTCC ပ O ω AACTAACTAG Ω ATGGGTTGGA TACCCAACCT > 3 1701 2

GGAACCCTGG CCTTGGGACC GCGTGCTGAG GACACTGCCG TCTATTATTG TGCTCGAGAC ACGGCCGCTT ACTTCGACTA CTGGGGTCAA GACCCCAGTT O ပ TGAAGCTGAT Ω [z. TGCCGGCGAA ~ Ø AGATAATAAC ACGAGCTCTG Ω α: æ O >• >• CTGTGACGGC æ E CGCACGACTC (T) 4 1801 TACCTGCAGA TGAACAGCCT ACTTGTCGGA ഗ z ATGGACGTCT 103

CGACGGACCA GCTGCCTGGT O GCGCCCTGG CGCCGGGACC Ø ď TGGGGGCACA ACCCCCGTGT E ပ ပ CCCTCCTCCA AGAGCACCTC TCTCGTGGAG တ ₽ S GGGAGGAGGT 1 S တ CCCCCTGGCA GGGGGACCGT 4 ᆸ Δ, CATCGGTCTT GTAGCCAGAA (z, > S ACCAAGGGCC TGGTTCCCGG ဗ × CTCGGCCTCC GAGCCGGAGG တ ø S AGTGGCAGAG TCACCGTCTC ഗ > 1901 137

GAGTCCTGAG CTCAGGACTC G တ TCCTACAGTC AGGATGTCAG AAGGGCCGAC TTCCCGGCTG 4 Δ, CGTGCACACC GCACGTGTGG E⊸ I > TGACCAGCGG AGTCCGCGG ACTGGTCGCC တ H TCAGGCGCCC Æ, Ö GTCGTGGAAC CAGCACCTTG z 3 ഗ CGGTGACGGT GCCACTGCCA H AAGGGGCTTG TTCCCCGAAC ω ۵, GTTCCTGATG CAAGGACTAC Ω ×

CAGCAACACC AAGGTGGACA TICCACCTGT Greenge GACCTACATC TGCAACGTGA ATCACAAGCC CTGGATGTAG ACGTTGCACT TAGTGTTCGG × = > z ပ GACTGTGCCC TCTAGCAGCT TGGGCACCCA ACCCGTGGGT O ₽ Ö CTGACACGGG AGATCGTCGA ഗ တ ഗ Ω, > 2101 TACTCCCTCA GCAGCGTGGT CGTCGCACCA > > S ATGAGGGAGT L 203

GICTICCICI ICCCCCCAAA AGGGGGGTTT CAGAAGGAGA CCCTGGCAGT GGGACCGTCA တ Q, Ö CCAGCACCTG AACTCCTGGG GGTCGTGGAC TTGAGGACCC ... Œ Ω, Æ d TGTGACAAA CTCACACATG CCCACCGTGC GGGTGGCACG O Δ, ۵, GAGTGTGTAC ۲ ACACTGTTTT Δ O GCCCAAATCT CGGGTTTAGA တ × AGAAAGTTGA TCTTTCAACT × 2201 237

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GACCATGCAC CTGGTACGTG TCAAGTTCAA AGTTCAAGTT [z, GAGCCACGAA GACCCTGAGG CTGGGACTCC ω ρ. CTCGGTGCTT ш = TGGTGGACGT ACCACCTGCA > Ω > CCCTGAGGTC ACATGCGTGG GGGACTCCAG TGTACGCACC ပ (L) ACCCAAGGAC ACCCTCATGA TCTCCCGGAC AGAGGGCCTG œ S TGGGAGTACT Σ .\_ ۲ IGGGTTCCTG 2301 270

GTGGTCCTGA CACCAGGACT Ω 0 CACCGTCCTG GTGGCAGGAC H > E TCAGCGTCCT AGTCGCAGGA ы > ഗ TACCGTGTGG GTTGTCGTGC ATGGCACACC > œ > CAACAGCACG E-တ z AGGAGCAGTA TCCTCGTCAT O ш AAGCCGCGGG Tregecece œ Δ, TGCCAAGACA ACGGTTCTGT ۲ × A, GACGCCTGG AGGTGCATAA TCCACGTATT = CTGCCGCACC ω Ö Ω 2401 303

CCCGAGAACC GGCTCTTGG ω æ AAAGGGCAGC Trirecegree O G CTCCAAAGCC GAGGTTTCGG æ × ഗ GCCCCCATCG AGAAACCAT TCTTTTGGTA E→ × CGGGGGTAGC Œ Н Δ, AGCCCTCCCA TCGGGAGGGT Ω, H 4 TCTCCAACAA TTCACGTTCC AGAGGTTGTT × z တ AAGTGCAAGG × ပ CAAGGAGTAC GTTCCTCATG > ш × CCGACTTACC GGCTGAATGG z 2501 337

CATCGCCGTG GTAGCGGCAC CTGCCTGGTC AAAGGCTTCT ATCCCAGCGA TAGGGTCGCT ഗ GACGGACCAG TTTCCGAAGA Œ, Ö > . O AGAGATGACC AAGAACCAGG TCAGCCTGAC AGTCGGACTG E٠ H တ TTCTTGGTCC O z TCTCTACTGG ₽ Σ ω CATCCCGGGA GTAGGGCCCT ω o: ഗ ACCCTGCCCC TGGGACGGG ρ, H ACAGGTGTAC TGTCCACATG > > O 2601 370

CTCACCGTGG GAGTGGCACC CTACAGCAAG GATGTCGTTC တ TCCGACGCT CCTTCTTCCT GGAAGAAGGA Çz, Œ AGGCTGCCGA G Ω CGTGCTGGAC GCACGACCTG Ω u > CCACGCCTCC GGTGCGGAGG ρ. ρ, ₽ AACTACAAGA TTGATGTTCT ₽ × × GCCGGAGAAC CGCCTCTTG z ы ۵, GCAATGGGCA CGTTACCCGT ပ z GAGTGGGAGA CTCACCCTCT ω 3 ω 2701 403

TCTCATGCTC CGTGATGCAT GAGGCTCTGC ACAACCACTA CACGCAGAAG AGCCTCTCCC TGTCTCCGGG ACAGAGGCCC TCGGAGAGGG GTGCGTCTTC × O ₽ TGTTGGTGAT × z CTCCGAGACG H 4 ω GCACTACGTA ::: Σ > AGAGTACGAG S O GTGGCAGCAG GGGAACGTCT CCCTTGCAGA z CACCGTCGTC O O 3 2801 ACAAGAGCAG TGTTCTCGTC ഗ 437

CTATTCGAAA TAAATAAGCA TGCGACGGCC CTAGAGTCCC TAACGCTCGG TTGCCGCCGG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT CGAATAGTAG ATTTATTCGT ACGCTGCCGG GATCTCAGGG ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAATTGAG TACAAACTGT × 2901

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TCTCAGCTTA AAAAAGAAGA TTTTTCTTCT GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC CAACAATAAA TTCGAACGGG CITAAGITIGA AGAGGIATGA AACCIAITICC ITIAIGICIG IACTITITIAG AGIAACGACI GAACTGTGTG CGCAGGTAGA 101

CAGGTAGAGG GTTGATTGAT CAACTAACTA AGCITTIGGAG ATTATCGICA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG CITGACACAC GCGICCAICI ICGAAACCIC IAATAGCAGI GACGITACGA AGCGITATAC CGCGITITAC IGGITGICGC

CTCGTCAGTA AACITICGTAG GAGCAGTCAT TTGAAGCATC CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAGGAGGTTA GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT CGAGGTAAAG GCTCCATTTC GGCGCTGTA CCCGCGACAT 201

GTACGCAAGT CATGCGTTCA TTTGTAACTA CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT TITITAATGIA ATAGTCGCTT TGTTTTTATT GCTGTCATAA AGTTGTCACG GCCGAGACTT AAAAGTTAAT CTTTTCAACA TITICAATTA GAAAGTIGI 301

CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG TIGCATCIAI GITCGITITI ICIAITGCIA CAAACGCGIA CGCIGAIAIC Δ anti-tissue factor light chain E Ē, > [z, TITCITATAG CGTAAAGAAG AACGTAGATA တ Þ Ä TCACGTAAAA AGGGTATCTA GAATTATGAA AAAGAATATC GCATTTCTTC .-Start STII signal TIR 7 × TCCCATAGAT CITAATACIT AGTGCATTTT 401

GACTTGACCA TGCAGAGCCA GTCGCGACAT CAAGAGCTAT CTGAACTGGT 3 z GTTĊTCGATA ഗ × CAGCGCTGTA Ω œ ACGTCTCGGT Ø œ CACCATCACC GTGGTAGTGG ₽ CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CGCTATCCCA œ Ω CGGAGACACC G ഗ GAGGGACAGG ഗ ᆈ ഗ AGTCCCCGAG TCAGGGGCTC ഗ ρ, ഗ CAGATGACCC GTCTACTGGG Σ o 501 56

GTTCTGGGAC CAAGACCCTG G GCTCCGAAAG TACTGATITIA CTATGCTACT AGTCTCGCTG AAGGAGTCCC TTCTCGCTTC TCTGGATCCG TTCCTCAGGG AAGAGCGAAG AGAGCTAGGC တ Œ, œ တ ρ, > ဗ TCAGAGCGAC æ S GATACGATGA Ø >-ATGACTAAAT **≻**+ H CGAGGCTTTC × ρ, æ ACCAGGAAAA TGGTCCTTTT × G Д ATCAACAGAA TAGTTGTCTT O O 601 9

ACAGGGTACC TGTCCCATGG ပ O GGACATTTGG CCTGTAAACC Ö (z, GAGTCTCCAT CTCAGAGGTA 3 Δ, S GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA AGTCGTGCCT Ö × O AAGCGTTGAA TAATGACAGA ပ >-> ₽ A H CGGTCTTCTG Ω ω CGTCAGACGT ... တ GACTGGTAGT ₽ CCTAATGTGA 701 8

CACACGGACG GTGTGCCTGC ပ TGCTTCTGTT ACGAAGACAA ഗ AATCTGGAAC TTAGACCTTG Ö ഗ GAGCAGTTGA CGGTAGACTA CTCGTCAACT ... o GCCATCTGAT Ω ഗ ρ, TCATCTTCCC GGTAGACAGA AGTAGAAGGG ᅜ CCATCTGTCT S AGTITIGCTIG ACACCGACGI TCAAACGAAC TGTGGCTGCA 4 > ø 801 AAGGTGGAGA TTCCACCTCT × 126

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GTCACAGAGC AGGACAGCAA GGGCCTGAGC ഗ CAGTGTCTCG TCACCCATCA CCAGGAGAGT GGTCCTCTCA GCCTGCGAAG ы ø GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC CAAAGTCTAC GCCCATTGAG ပ CGGGAGGTTA ACGAGAAACA 0 ... CCACCTATTG AAAGCAGACT Ω > GACGCTGAGC ATGTCACCTT 3 o CTCCGGTTTC GCAGCACCCT × Ø CTATCCCAGA GATAGGGTCT TACAGCCTCA œ ۵, TGAATAACTT GGACAGCACC ACTTATTGAA z z 901 1001 160

CCCGGACTCG တ .-AGTGGGTAGT × CGGACGCTTC Œ ບ GTTTCAGATG > × TGCTCTTTGT = × ш TTTCGTCTGA Ω æ CTGCGACTCG တ ., ₽ CGTCGTGGGA E٠ တ ATGTCGGAGT ... S CCTGTCGTGG တ Ω 193

AGGCCTAACG TCCGGATTGC AGCTCGGTAC CCGGGGATCT CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA CATCGTGGCG ACCCCCCACG TAAATCCTCT GAGTGTTAAT 0 ပ CAACAGGGGA GITGICCCCT G 24 z GTTTCTCGAA CAAAGAGCTT Cz, ഗ AGCGGGCAGT TCGCCCGTCA > ρ, တ 1101 226

lambda to terminator

AGCTGTGGTA GOCGTCAGGC AGCCATCGGA TCGGTAGCCT CCGCAGTCCG ITITIATIGIT GCGACGCGC ATCTCGACTG CACGGTGCAC CAATGCTTCT GTTACGAAGA CGGCCCGCAA AAATAACAA CGGCTGCGCG TAGAGCTGAC GTGCCACGTG creserrece secesecerr SAGCCAACGG 1201

ACATCATAAC GGTTCTGGCA TGTAGTATTG CCAAGACCGT CACTGCATAA TICGIGICGC ICAAGGCGCA CICCCGITICI GGATAAIGIT ITTTGCGCCG CCAGCATTTA GTGACGTATT AAGCACAGCG AGTTCCGCGT GAGGGCAAGA CCTATTACAA AAAACGCGGC GGTCGTAAAT TGGCTGTGCA ACCGACACGT 1301

TTATAAGACT TTACTCGACA ACTGTTAATT AGTAGCTTGA TCAAATTACA CACCTTAACA CTCGCCTATT GTTAATTCGA ATCCTAGATC TTAATACTTC 1401 AATATTCTGA AATGAGCTGT TGACAATTAA TCATCGAACT AGTTTAATGT GTGGAATTGT GAGCGGATAA CAATTAAGCT TAGGATCTAG AATTATGAAG

Start STII signal TIR 3

O CCGGACCACG 1501 AAGAATATTG CGTTCCTACT TGCCTCTATG TTTGTCTTTT CTATAGCTAC AAACGCGTAC GCTGAGGTTC AGCTGGTGGA GTCTGGCGGT GGCCTGGTGC > ... CAGACCGCCA G Ö ഗ GCAAGGATGA ACGGAGATAC AAACAGAAAA GATATCGATG TTTGCGCATG CGACTCCAAG TCGACCACCT 臼 > .\_ > e a heavy chain with cys to ser in hinge NAY IAT [4 > anti-tissue factor Σ ഗ 4 ᆸ TTCTTATAAC z

GCCCCGGGTA AGGGCCTGGA TCCCGGACCT . CGGGGCCCAT Ö GGTCCGTCAG CCAGGCAGTC O œ > CTTCAATAIT AAGGAGTACT ACAIGCACTG TGTACGTGAC I Σ TTCCTCATGA >ω GAAGTTATAA z ſz, CAGCTTCTGG GTCGAAGACC Ö S 4 TTGTCCTGTG AACAGGACAC ပ တ GAGTGAGGCA CTCACTCCGT æ u S 1601 AGCCAGGGG regereeee G O Q, 37

## FIG. 7B

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TTTGTGTCGI H CCGTGCCACT ATAAGCGCTG ACAATTCCAA GGCACGGTGA TATTCGCGAC TGTTAAGGTT ဟ CAACACGATC TATGACCCGA AGTTCCAGGA TCAAGGTCCT O Œ, ATACTGGGCT ρ, Δ >-GTTGTGCTAG . **⊱**⊣ z TTGATTGATC CAGAGCAAGG GTCTCGTTCC G O ш AACTAACTAG Ω 1701 ATGGGTTGGA TACCCAACCT ပ 3

GGAACCCTGG CCTTGGGACC u H CTGGGGTCAA GACCCCAGTT O G GCGTGCTGAG GACACTGCCG TCTATTATTG TGCTCGAGAC ACGGCCGCTT ACTTCGACTA TGAAGCTGAT Ω TGCCGGCGAA Ø T A CTGTGACGGC AGATAATAAC ACGAGCTCTG Ω œ ⋖ >->-> ⋖ €→ Δ CGCACGACTC 回 Ø œ TGAACAGCCT ACTIGICGGA တ z TACCTGCAGA ATGGACGTCT O **>**-1801 103

CGACGGACCA GCTGCCTGGT u O GCGGCCCTGG CGCCGGGACC ဗ 4 TGGGGGCACA TCTCGTGGAG ACCCCCGTGT ₽ Ö ဗ AGAGCACCTC ഗ H တ CCCCTGGCA CCCTCCTCCA GGGAGGAGGT × ഗ လ ۵, GGGGGACCGT ø .\_ ρ, CATCGGTCTT GTAGCCAGAA > ഗ 1901 TCACCGTCTC CTCGGCCTCC ACCAAGGGCC TGGTTCCCGG ပ × GAGCCGGAGG တ æ ഗ AGTGGCAGAG 137

CTCAGGACTC GAGTCCTGAG u Ö ഗ Trecedent retracagre AGGATGTCAG AAGGGCCGAC Δ, CGTGCACACC GCACGTGTGG ₽ => TCAGGCGCCC TGACCAGCGG AGTCCGCGG ACTGGTCGCC O S ₽ 4 O GTCGTGGAAC CAGCACCTTG z 3 S CGGTGACGGT GCCACTGCCA E > TTCCCCGAAC AAGGGGCTTG Q, E4) Ω, GTTCCTGATG CAAGGACTAC Ω × 2001 170

AAGGTGGACA TTCCACCTGT CAGCAACACC GTCGTTGTGG z TGCAACGTGA ATCACAAGCC TAGTGTTCGG ρ, ×  $\equiv$ ACGTTGCACT > z O CTGGATGTAG GACCTACATC -Y L TGGGCACCCA ACCCGTGGGT O H ပ TCTAGCAGCT CTGACACGGG AGATCGTCGA S တ တ GACTGTGCCC ۵, > ₽ GCAGCGTGGT CGTCGCACCA > S ATGAGGGAGT TACTCCCTCA ... ഗ >-2101 203

TCCCCCCAAA GICTICCICT CAGAAGGAGA (IL GGGACCGTCA CCCTGGCAGT ۵, O CTCACACTAG TCCACCGTCT CCAGCACCTG AACTCCTGGG GAGTGTGATC AGGTGGCAGA GGTCGTGGAC TTGAGGACCC ... .-ഗ Δ, TGTGACAAAA ACACTGTTTT Ω GCCCAAATCT CGGGTTTAGA × AGAAAGTTGA TCTTTCAACT 2201 237

ser ន Alinge cys \*Hinge cys to ser

CTGGTACGTG GACCATGCAC 3 GACCCTGAGG TCAAGTTCAA CIGGGACTCC AGTICAAGTT (z, CCCTGAGGTC ACATGCGTGG TGGTGGACGT GAGCCACGAA CTCGGTGCTT I ഗ GGGACTCCAG TGTACGCACC ACCACCTGCA Ω > > ပ 臼 ۵, TCTCCCGGAC AGAGGGCCTG œ TGGGAGTACT ACCCAAGGAC ACCCTCATGA TGGGTTCCTG × 270

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CACCGTCCTG CACCAGGACT GTGGTCCTGA Ω GTGGCAGGAC H ₽ CAACAGCACG TACCGTGTGG TCAGCGTCCT GTTGTCGTGC ATGGCACACC AGTCGCAGGA L > S > œ တ Z TGCCAAGACA AAGCCGCGGG AGGAGCAGTA TTCGGCGCCC TCCTCGTCAT O ш œ ACGGTTCTGT × 2401 GACGCCTCC AGGTCCATAA TCCACGTATT × CTGCCGCACC G Ω 303

CCCGAGAACC GGCTCTTGG (LI) œ AAAGGGCAGC TTTCCCGTCG œ CTCCAAAGCC GAGGTTTCGG 4 × တ AGAAAACCAT TCTTTTGGTA ۴ GCCCCCATCG CGGGGGTAGC Н ρ. æ AGCCCTCCCA TCGGGAGGGT Ω, ... 4 TCTCCAACAA AGAGGTTGTT × . Z တ TTCACGTTCC AAGTGCAAGG × U CAAGGAGTAC GTTCCTCATG >ω GGCTGAATGG CCGACTTACC ပ z 2501 337

CATCGCCGTG GTAGCGGCAC æ ATCCCAGCGA TAGGGTCGCT CTGCCTGGTC AAAGGCTTCT TTTCCGAAGA Œ ပ GACGGACCAG > -1 O AAGAACCAGG TCAGCCTGAC AGTCGGACTG E ... ഗ TTCTTGGTCC o z AGAGATGACC TCTCTACTGG H Σ Œ CATCCCGGGA GTAGGGCCCT ഠ 2 တ ACCCTGCCCC TGGGACGGG Q, H TGTCCACATG ACAGGTGTAC > 2601

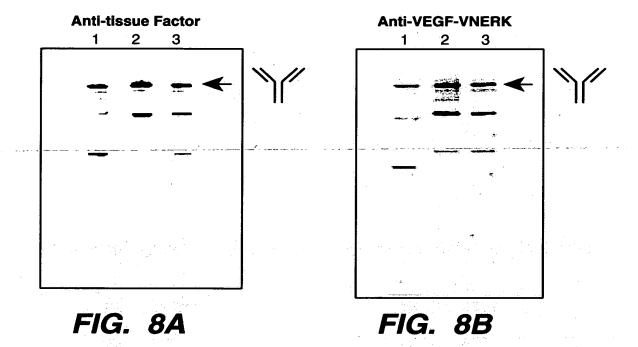
CTCACCGTGG GAGTGGCACC GATGTCGTTC CTACAGCAAG တ CCTTCTTCCT GGAAGAAGGA Œ, Cz. CGTGCTGGAC TCCGACGGCT AGGCTGCCGA Ö Ω GCACGACCTG Ω ... > CCACGCCTCC GGTGCGGAGG Ω, AACTACAAGA TTGATGTTCT × GCAATGGGCA GCCGGAGAAC CGCCTCTTG z Œ Δ CGTTACCCGT ပ GAGTGGGAGA CTCACCCTCT ω 3 凹 2701 403

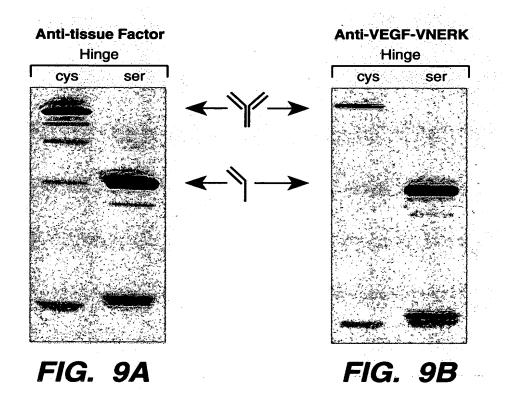
GIGGCAGCAG GGGAACGICT ICTCAIGCIC CGIGAIGCAT GAGGCICIGC ACAACCACIA CACGCAGAAG AGCCICICCC IGICICGGG ACAGAGGCCC TCGGAGAGGG ഗ GTGCGTCTTC O CTCCGAGACG TGTTGGTGAT × z H Ø Œ GCACTACGTA × Σ AGAGTACGAG O တ CCCTTGCAGA > z CACCGTCGTC O O 3 2801 ACAAGAGCAG TGTTCTCGTC œ ഗ 437

CTATTCGAAA TAAATAAGCA TGCGACGGCC CTAGAGTCCC TAACGCTCGG TTGCCGCCGG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT CGAATAGTAG ACGCTGCCGG GATCTCAGGG ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAATTGAG TACAAACTGT ATTTATTCGT × 2901

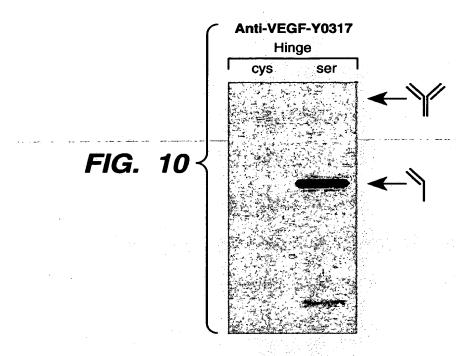
## FIG. 7D

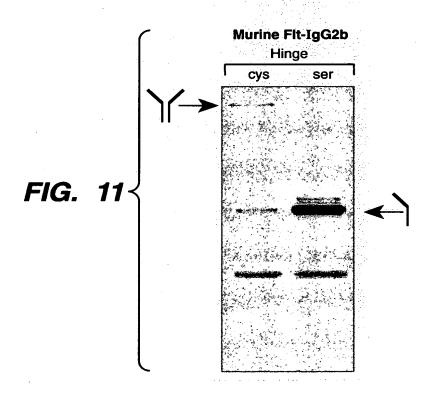
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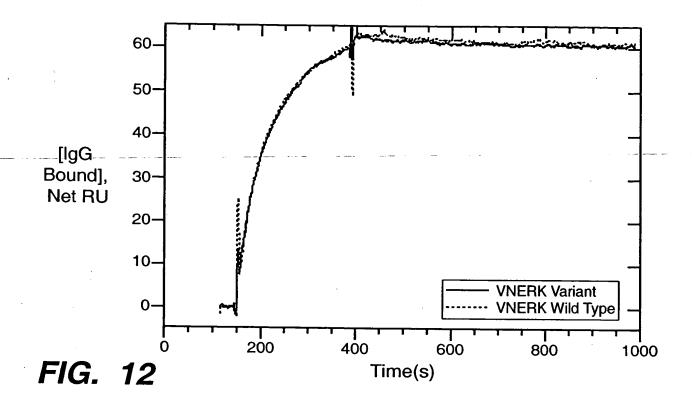
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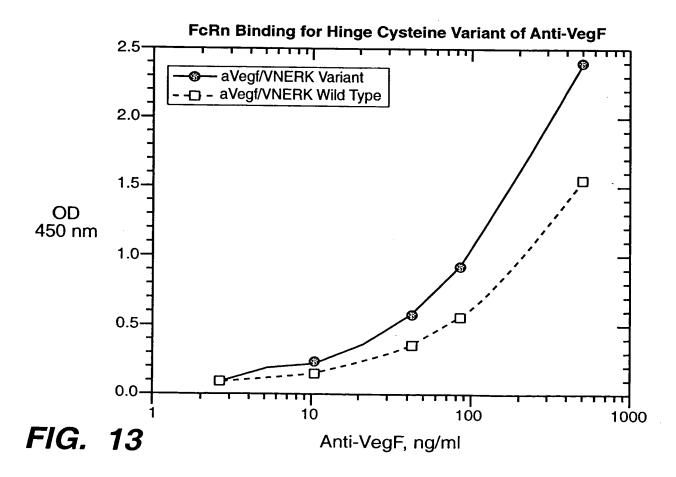




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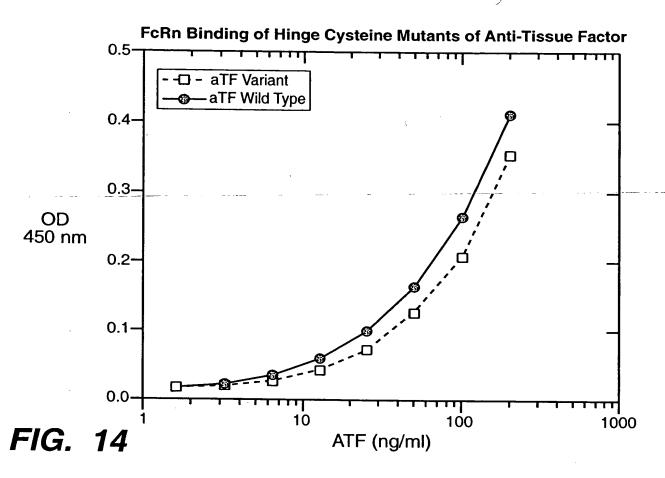
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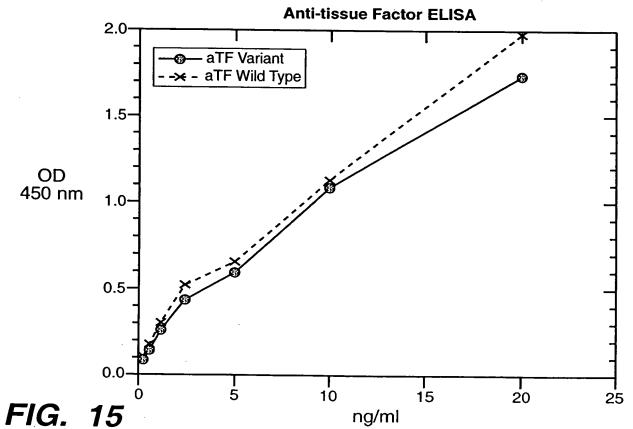




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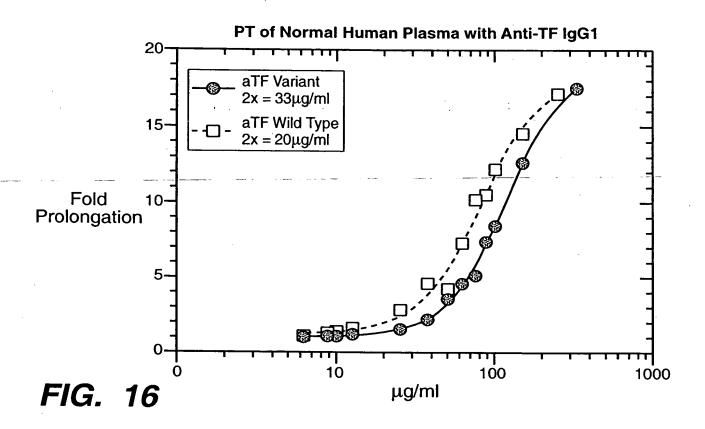


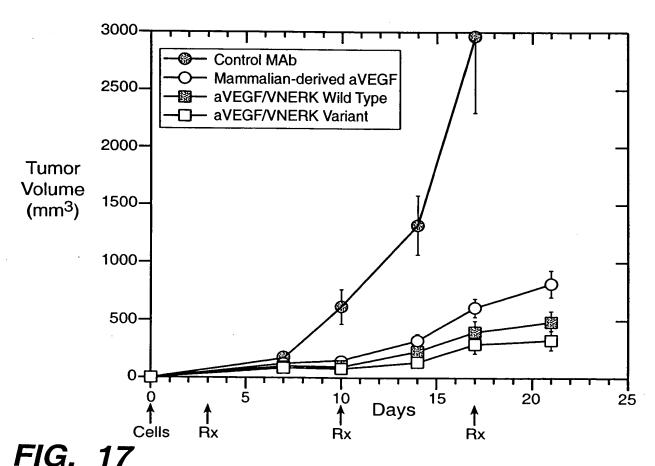


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